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Environmental Toxins Guide

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Disclaimer

Educational material is for informational purposes only and is not intended to be a substitute for medical advice from a healthcare practitioner. The statements in this report have not been evaluated by the Food and Drug Administration and are only meant to be lifestyle choices for potential risk mitigation. Please consult your physician for medication, treatment, diet, exercise or lifestyle management as appropriate. This product is not intended to diagnose, treat, or cure any disease or condition.

What are Environmental Toxins?

Environmental toxins are ubiquitous in today's society. The rate of toxin exposure is growing due to increased production and bioaccumulation that occurs from various chemicals. The amount of toxic chemicals released into the environment is growing exponentially over the years. In 1994, the US released 2.2 billion pounds, which grew to 4.7 billion pounds in 2002[1]. The EPA inventory contains roughly 84,000 chemical substances that are in commerce, many of which have limited testing for their effects on humans or the environment[2]. Chemicals no longer authorized for use in the U.S. (e.g., DDT) continue to persist in the environment as persistent organic pollutants. One study identified almost 200 chemicals in neonate cord blood, underlying the significant exposure pregnant women have to toxins. This is especially concerning due to the risk for developmental disorders (amongst other health effects) many of them have[3]. We have an environmental toxin problem.

The toxic burden endured by the body encompasses the amount of toxic substances and metabolites that accumulate. Depending on the type of environmental chemical, some are rapidly broken down and metabolized quickly, while others are fat soluble, bioaccumulate in tissues and are poorly broken down. It's important to note the concept of synergistic toxicity, whereby multiple environmental toxins can contribute to added negative physiological effects. If a high burden is also combined with decreased detoxification processes from nutrient deficiencies, impaired elimination or genetic SNPs, there may be an exacerbation of the health effects due to prolonged toxin impact. This is where bio-individuality is extremely important in understanding each person's susceptibility to environmental toxicants. Increased levels of toxins can overburden the body's ability to detoxify adequately, leading to excess accumulation in the body (particularly in fatty tissues like adipose, brain, etc.) and potentially increased toxic reactive intermediates from phase 1 activities.

Toxin exposures have been associated with many medical conditions/disease states. The risk varies based upon quantity of toxicant exposure, length of time exposed, genetic susceptibility, synergistic effects with other toxicants, and factors that influence detoxification pathways. Common areas of concern include cancer, cardiovascular disease, neurological disorders, immune dysfunction, developmental disorders, negative reproductive effects, hormonal imbalances, and a host of relevant symptoms and negative health outcomes. It is believed that most people are dealing with a toxic burden at some level, it's just a matter of how much that toxic burden is contributing to somebody's current symptoms or disease state.

Understanding the potential risks associated with environmental toxins allows individuals to be proactive with their health. The first step is understanding what an individual is being exposed to consistently and what those levels are. A urinary environmental toxicant test will identify chemicals of concern. Once they have been identified, it's extremely important to decrease exposure by identifying sources, making changes to products used (if necessary), and making other changes based on the chemical. It's also important to support all phases of the body's natural detoxification processes, phase 1, phase 2, phase 3 and to support the elimination of these toxicants from the body. This can be accomplished through dietary changes, nutrient/supplement interventions and other specific modalities. Other tests may be helpful when completed in conjunction with the Environmental Toxin test to assess the physiological impact from exposure as well as factors that may affect detoxification abilities. The benefit to assessing environmental toxins via a simple urine testing is to allow an individual to understand risk factors that may significantly impact their health and allow them to take actionable steps to decrease their risk and hopefully improve health outcomes.

Environmental Toxin Protocol

1

IDENTIFY & REMOVE SOURCES OF EXPOSURE

The first step is to understand what toxic chemicals are elevated and to remove those sources of exposure

***See sources and exposure for each toxin/metabolite

2

SUPPORT EXCRETION PATHWAYS

Focus on improving excretion and drainage pathways before upregulating detoxification processes

***See recommendations on pages 52-53 to improve excretion pathways

3

SUPPORT PHASE 2 DETOXIFICATION

Focus on specific conjugation pathways for each toxin

***See recommendations on pages 54-55 to upregulate conjugation pathways

4

SUPPORT PHASE 1 DETOXIFICATION

Focus on increasing or decreasing phase 1 detoxification depending on the patient

***See recommendations on pages 57-58 to support phase 1 detoxification

5

MINIMIZE RISK FROM EXPOSURE

Incorporate strategies to offset risk from toxic exposure

***See recommendations on page 59

PESTICIDES

Pesticides are a group of chemicals used for the destruction of insects, weed, fungi, bacteria, etc. There are many categories of insecticides based on their chemical nature, including: organochlorines, organophosphates, carbamates, pyrethroids, etc.

Tested markers:

- Organochlorine Pesticides: DDT
- Organophosphate Pesticides
- Pyrethroid Pesticide: 3PBA

Organochlorine Pesticide: DDT

Marker Tested: DDA (2,2-bis(4-chlorophenyl)-acetic acid)

CATEGORIZATION

Metabolite: DDA (2,2-bis(4-chlorophenyl)-acetic acid)

Parent Chemical: DDT

Category: Organochlorine Pesticide

GENERAL INFO

DDT was used an insecticide in agriculture and the control of vector-borne disease but was banned in the US in 1972[4]. Some countries still use DDT to control mosquitos for malaria spread[4]. Highest levels used in India, North Korea, Ethiopia, Namibia, South Africa and other African countries[5]. DDT is categorized as a persistent organic pollutant (POP), leading to high bioaccumulation in the body and the environment.

EXPOSURE & SOURCES

- DDT can be found in soil, water, or air and has the ability to travel long distances from the original source[6]
- DDT can be found in various foods such as meat, poultry, fish, and dairy products, likely due to it acting as a POP and due to bioaccumulation in animals[6]
- The FDA and USDA have reported detectable levels of DDT and metabolites in American cheese, butter, catfish, carrots, summer squash and salmon[6]
- Foods imported from countries still using DDT may contain higher levels of DDT[7]

PHYSIOLOGICAL EFFECTS

- DDT is a POP that accumulates in fatty tissue and has been classified as a B2 carcinogen for humans[8]
- DDT's mechanism of action involves interfering with normal nerve impulses in the nervous system[7]
- DDT exposure in humans may play a role in the aetiology of conditions such as pancreatic cancer, neuropsychologi-caldys function and reproductive outcomes[9]
- Animal studies with chronic exposure showed increased development of liver tumors, sterility, kidney inflammation, tremors with death, the higher mortality in rat offspring[6,7]

GENERAL CONSIDERATIONS

- Limit consumption of foods from countries actively using DDT
- Consider using filtered water
- Increase aerobic exercise: Animal studies showed exercise can reduce DDT-induced oxidative damage and promote DDT degradation[10]

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Animal studies show DDT induces CYP2B and CYP3A, and to a lesser extent CYP2B[11]
- **Phase 2:** Glutathione conjugation via glutathione S transferases (GSTs)[12]
- **Excretion:** Urine; the major route of excretion is as DDA conjugates in the urine[11]
- **Other:**
  - Animal studies show supporting serotonin may help increase tolerance to DDT's neurotoxic effects[13]
  - Animal studies show antioxidant support from ascorbic acid may induce antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione S-transferases (GSTs), increasing defense against DDT
  - The ½ life of DDT is roughly 7-8 years[14]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

7

Organophosphate Pesticides

Markers Tested: DEDTP, DMDTP, DETP, DMP, DEP, DMTP

CATEGORIZATION

Metabolites: Diethyldithiophosphate (DEDTP), Dimethyldithiophosphate (DMDTP), Diethylthiophosphate (DETP), Dimethylphosphate (DMP), Diethylphosphate (DEP), Dimethylthiophosphate (DMTP)

Parent Chemical: Multiple chemicals (See chart on next page)

Category: Organophosphate pesticide

GENERAL INFO

- Organophosphate pesticides (OPs) are the most commonly used class of insecticides in the United States[15]
- OPs are typically used in agriculture to control pests on various crops, but they are also used for pest control in domestic or commercial areas or on domestic animals[15]

EXPOSURE & SOURCES

- **Absorption:** Commonly occurs with occupational exposure via dermal absorption or inhalation with individuals applying pesticides or via the oral route from food contamination
    - Neighboring areas may have increased exposure in air and dust due to spray drift from aerial (airplane) application, which can affect significant distances
- **Agricultural use on food:** corn, alfalfa, sorghum, sunflower, wheat, grapes, citrus, cotton, soybeans, and other foods[15]
- **Home pest control products, including head lice treatment products**
- **Flea and tick control products for pet/livestock:** collars, shampoos, sprays, powders[16]

PHSYIOLOGICAL EFFECTS

- Some OPs are classified by International Agency for Research on Cancer as probably carcinogenic to humans (group 2A), while others are listed as possibly carcinogenic to humans (group 2B)[17]
- Functions as an acetylcholinesterase inhibitor and can have significant impact on neurological function
- Adverse birth and neurodevelopmental outcomes, reduced birth weight and length, shorter gestational duration, increased number of abnormal reflexes, higher risk of reported attention problems and lower intelligence[18]
- OP exposure is significantly positively associated with non-hodgkin's lymphoma risk[19] as well as an increased risk for other cancers such as lung cancer, prostate cancer, breast cancer, ovarian cancer and thyroid cancer[17]
- OP exposure has been associated with metabolic changes linked to obesity, type 2 diabetes,[20] and endocrine disruption[21]

GENERAL CONSIDERATIONS

- Neurotransmitter test to assess acetylcholine levels
- Choose organic produce as able
    - One study involving 16 participants found that an organic diet significantly reduced the urinary excretion of several pesticide metabolites and parent compounds[22]
    - Another study in 23 elementary school-age children showed a dramatic and immediate protective effect against exposure to organophosphate pesticides after adopting an organic diet for the 15-day study[23]
- Wash produce before eating
- Use pesticide free pest control for home and garden[15]; Use bait and traps instead of sprays
- Decrease "take home pathways" from aerial spray drift by changing clothes and taking off shoes prior to entering home
- Use filtered water

DETOXIFCATION CONSIDERATIONS

- **<u>Phase 1:</u>** Many OP chemicals act as Cytochrome P450 inhibitors Phase 2: Glutathione conjugation via glutathione S transferases (GSTs)[12]
    - Chlorpyrifos is a significant inhibitor of CYP1A and a moderate inhibitor of CYP2C and CYP3A[24]
- **<u>Phase 2</u>:** Glutathione conjugation[25]; PON1 enzyme can detoxify OPs
- **<u>Excretion:</u>** Urine; animal studies demonstrate the main route of OP excretion is via urine[26]
- **<u>Other:</u>**
    - Animal studies show that Lactobacillus Rhamnosus may help in reducing toxic organophosphate pesticide exposure by passive binding[27]
    - Animal models show Lactobacillus Casei may decrease organophosphate pesticide induced cytotoxicity[28]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

OP Metabolites & Chemicals

*** = Highly Toxic **= Moderately Toxic	DEDTP	DMDTP	DETP	DMP	DEP	DMTP
Phorate*** *(Thimet, Rampart, AASTAR)*	x		x		x	
Terbufos*** *(Counter, Contraven)*	x		x		x	
Disulfoton*** *(Disyston)*	x		x		x	
Ethion** *(Ethanox)*	x		x		x	
Azinphos-methyl*** *(Guthion, Gusathion)*		x		x		x
Dimethoate** *(Cygon, DeFend)*		x		x		x
Malathion** *(Cythion)*		x	x	x		
Methidathion*** *(Supracide, Ultracide)*		x		x		x
Phosmet** *(Imidan, Prolate)*		x		x		x
Chlorethoxyphos			x		x	
Chlorpyrifos** *(Durban, Lorsban, Brodan) (discontinued for home use)*			x			
Coumaphos*** *(Co-Ral, Asuntol)*			x		x	
Diazinon** *(Spectracide)*			x		x	
Parathion*** *(discontinued)*			x		x	
Sulfotep*** *(Thiotepp, Bladafum, Dithione)*			x		x	
Chlorpyrifos methyl*** *(Durban, Lorsban, Brodan) (discontinued for home use)*				x	x	x
Dichlorvos** *(DDVP, Vapona)*				x		
Dicrotophos				x		
Fenitrothion** *(Accothion, Agrothion, Sumithion)*				x		x
Fenthion** *(Mercaptophos, Enter, Baytex, Tiguvon)*				x		x
Isazophos-methyl				x		x
Methyl parathion*** *(E601, Penncap-M)*				x		x
Oxydemeton-methyl** *(Metasystox-R)*				x		x
Pirimiphos-methyl** *(Actellic)*				x		x
Temephos** *(Abate, Abathion)*				x		x
Naled** *(Dibrom)*				x		
Tetrachlorvinphos** *(Gardona, Apex, Stirofos)*				x		

Chart references[29,30]

Pyrethroid Pesticides

Marker Tested: 3-Phenoxybenzoic Acid (3-PBA)

CATEGORIZATION

Metabolite: 3-Phenoxybenzoic Acid (3-PBA)

Parent Chemicals: Cypermethrin, Permethrin, Deltamethrin, Cyhalothrin

Category: Pyrethroid Pesticides

GENERAL INFO

- Pyrethroid pesticides are used as insect pest control in agricultural and urban settings[31]
- Products containing pyrethroid pesticides usually end in either -thrin or -ate
- Pyrethroids are synthetic chemicals, but are based on naturally occurring pyrethrums found in the chrysanthemum plant

EXPOSURE & SOURCES

- **Insect control:** Pyrethroids can be used around the world to control for pests carrying infectious diseases, such as mosquito populations for malaria control
- **Agricultural use for food:** highest levels found in leaf vegetables, melons, beans, and root vegetables[32]
- **Water contamination** from agricultural or urban use
- Seafood, such as shrimp and other shellfish[32]
- **Pet care products:** to control fleas and ticks
- **Body care products:** treatment of lice and scabies, mosquito repellant products
- **Home and garden pest control products:** sprays for bedbugs, ticks, mosquitos

PHYSIOLOGICAL EFFECTS

- Increased risk for male reproductive dysfunction, childhood brain tumors, childhood acute lymphocytic leukemia, coronary heart disease, ADHD, impaired pulmonary function in children[32,33]
- Each 10-fold increase in 3-PBA levels detected in the urine of American children, showed a 50% increase in ADHD symptoms; boys were affected more than girls[34]
- Higher levels of pyrethroid pesticide exposure indicated by elevated urinary 3-PBA was associated with a higher risk of death from all causes or cardiovascular disease over an observational period of 14 years[35]
- Pyrethroid pesticide exposure can cause oxidative stress, inflammation, and DNA damage[35]

GENERAL CONSIDERATIONS

- Consume organic food as able
  - One study involving 16 participants found that an organic diet significantly reduced the urinary excretion of several pesticide metabolites and parent compounds[36]
- Wash produce before eating
- Consume filtered water
- Introduce natural predators for insect control in gardens (example-ladybugs to control aphids)

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Hydrolysis, hydroxylation & oxidation with CYP450[37]
  - Pyrethroid insecticides are known to be CYP inducers, but vary depending on the specific chemical used
  - Deltamethrin induces CYP3A4 and CYP2B6; Permethrin induced CYP to a lesser extent, but still induced CYP1A1, CYP3A4, CYP3A5, CYP2B6[38]
- **Phase 2:** Glucuronidation[39] and amino acid conjugation (glycine)[37]
- **Excretion:** Urine; 3-PBA is readily excreted in the urine, therefore urine levels are the best indicator of pyrethroid pesticide exposure[35]
  - Smaller amounts are excreted through the bile
  - The elimination half-life is roughly 8hrs, with 88% of the metabolite excreted within 24 hours after exposure[37]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

HERBICIDES

Herbicides are chemicals used to control the growth of weeds, herbs, and other undesirable vegetation.

Tested markers:

- Glyphosate
- Atrazine
- 2,4-D

Herbicide: Glyphosate

Marker Tested: Glyphosate

CATEGORIZATION

Metabolite: ⊘

Parent Chemicals: Glyphosate

Category: Herbicide

GENERAL INFO

- Glyphosate is an organophosphorus herbicide, but it has also been registered as a pesticide in the US since 1974[40]
- Glyphosate is not regularly tested for pesticide residues unlike other pesticides because it is generally considered to be safe

EXPOSURE & SOURCES

- **Agricultural use:** Highest levels found on glyphosate-resistant field crops (examples include- corn, wheat, soybeans, canola, alfalfa, cotton, sugar beets, sorghum)
- Dessication is a process where crops receive a dose of glyphosate prior to harvest: this often occurs with grains, seeds, and pulses
- **Water:** Contaminated water due to agricultural/at home use
- **Other sources:** Animal feed, home and garden weed control
- **Absorption:** Readily absorbed from the GI tract, respiratory tract and to a lesser extent through the skin

PHYSIOLOGICAL EFFECTS

- Disrupts microbiome and may induce antibiotic resistance in different organisms[41]
- Animal models show adverse effects throughout digestive system including decreased enzyme levels, disrupted microvilli structures, upper GI tract injury[42]
- May reduce nutrient levels: such as iron, magnesium, manganese, calcium & other trace metals due to its ability to chelate[42]
- Animal models show irreversible liver damage, elevated risk for kidney disease, increased lipid peroxidation & elevated TNF-α[42]
- Glyphosate acts as a glycine analogue, which may allow it to be incorporated into peptides when proteins are synthesized[43]

GENERAL CONSIDERATIONS

- Consume organic foods as able
- Choose products that have 'glyphosate residue free certification'
- Limit/avoid use of herbicides in the home garden
- Use filtered drinking water

DETOXIFICATION CONSIDERATIONS

- **Detoxification:** Glyphosate does not undergo significant metabolism and is excreted mostly unchanged as glyphosate[44]
  - Glyphosate is a known cytochrome P450 enzyme inhibitor[42]
- **Excretion:** Roughly two thirds of glyphosate is excreted in the feces as the unabsorbed parent compound, while most absorbed glyphosate is rapidly excreted in the urine as the parent compounds[44]
- **Other:**
  - Humic acid/fulvic acid may inhibit the antimicrobial effect of glyphosate on different bacteria[45]
  - Animal studies showed Ginkgo Biloba provided significant protection against glyphosate-induced toxicity[46]
  - Glycine supplementation may be supportive to counteract the negative effect of glyphosate on disrupting glycine homeostasis[47]
  - One animal study showed a combination of charcoal (200g) combined with either 500ml or sauerkraut juice or humic acid resulted in significant reduction of glyphosate in the urine (note: doses used were for animals in study and may need to be adjusted for humans)[48]
  - Vitamin C and Vitamin E have been shown to help to prevent against glyphosate induced cell damage[49]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Herbicide: Atrazine

Marker Tested: Atrazine & Atrazine Mercapturate

CATEGORIZATION

Metabolite: Atrazine Mercapturate

Parent Chemicals: Atrazine

Category: Herbicide

GENERAL INFO

- Atrazine is a type of herbicide called triazines, which is used predominantly in agriculture as a restricted use pesticide (RUP)
- Atrazine works by disrupting photosynthesis in plants
- Atrazine can be highly persistent in the environment, even more so in colder climates
  - Minimal adsorption to soil particles increases its ability to contaminate ground and surface waters[50]

EXPOSURE & SOURCES

- **Primarily used in agriculture** on various crops: commonly used on corn, sorghum, sugarcane, pineapple, macadamia nuts
- Neighboring areas may increase exposure
- **Water:** It is one of the most common pesticide contaminants in ground and surface water[50]
- It can persist in water sources for a long period of time
- High levels are found in the Midwest of the U.S.[51]
- **Other uses** include: residential lawns and golf courses, particularly in the southeast U.S., evergreen farms, and weeds on highways/railroads[52]

PHYSIOLOGICAL EFFECTS

- Animal studies show atrazine acts as an endocrine disruptor, resulting in hormone abnormalities, demasculinization in males, increased feminization, and decreased fertility[52]
- May increase risk of preterm birth[53]
- May increase risk of specific cancers including brain, testes, prostate, stomach, multiple myeloma and potentially cancer of estrogen-responsive tissues due to its ability to increase the 16α-OHE1/2-OHE ratio[54]

PHYSIOLOGICAL EFFECTS

- Consume filtered drinking water
- Assess quality/ contamination of well water (if applicable)
- Consider a whole house water filter or specific filters for bathing or showering
- Avoid/limit exposure to soils with recent atrazine application
- Caution swimming in bodies of water near areas using atrazine

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Dealkylation; CYP1A2 and CYP3A4 are primarily response responsible for phase 1 metabolism of atrazine in humans[55]
- **Phase 2:** Glutathione Conjugation & Methylation; Atrazine mercapturate is a metabolite of glutathione conjugation of atrazine[56]; It can also undergo methylation by methyltransferases to form other metabolites[57].
- **Excretion:** Primary route of detoxification is via urine. Atrazine is removed from the body relatively quickly, therefore urine levels typically reflect recent exposure within the past 24-48 hours[58].
- **Other:** Activated charcoal when taken with oral exposure to atrazine may decrease absorption[59]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Herbicide: 2,4-D

Marker Tested: 2,4-D

CATEGORIZATION

Metabolite: ⊘

Parent Chemicals: 2,4-D (2,4-dichlorophenoxyacetic acid)

Category: Herbicide

GENERAL INFO

- 2,4-D is a chlorophenoxy herbicide and can also be used as a plant growth regulator[60]
  - 2,4-D was first introduced in the US in the 1940s in a product called Agent Orange[61]

EXPOSURE & SOURCES

- Used for broadleaf weed control in agricultural and nonagricultural settings:
  - Uses include pasture, rangeland, residential lawns, roadways; often used in products labeled as 'weed and feed'
  - Main crops using 2,4-D include corn, soybeans, wheat, hazelnuts, sugarcane, and barley[60]
- Exposure can occur through food, water, dust, residential application, or contact/inhalation from spraying
- **Absorption:** The greatest absorption occurs from oral exposure, with dermal and inhalation to a lesser extent

PHYSIOLOGICAL EFFECTS

- Human study shows immunosuppressive effects from 2,4-D exposure[62]
- Human study showed increased risk for Parkinson's disease[63]
- Potential endocrine disruptor, particularly affecting the thyroid and gonads
- Other negative health effects include on reproduction, neurotoxicity, genetic mutations, etc.[64]
- IARC categorized 2,4-D as possibly carcinogenic to humans (group 2B) with a particular concern for non-hodgkins lymphoma[65]

GENERAL CONSIDERATIONS

- Use filtered water
- Choose organic foods as able
- Limit/avoid exposure to agricultural areas using herbicides

DETOXIFICATION CONSIDERATIONS

- **Detoxification:** Metabolism of 2,4-D is minimal and is largely excreted as the unchanged parent compound. Small amounts of 2,4-D may be excreted as an unspecified 2,4-D conjugate[66]
- **Excretion:** 2,4-D is rapidly excreted from the body via urine, in a dose-dependent non-linear manner[66]
  - Roughly 75% of 2,4-D is excreted within 96 hours of oral exposure[66]
  - Perspiration is another route of elimination, albeit slower than urinary excretion[66]

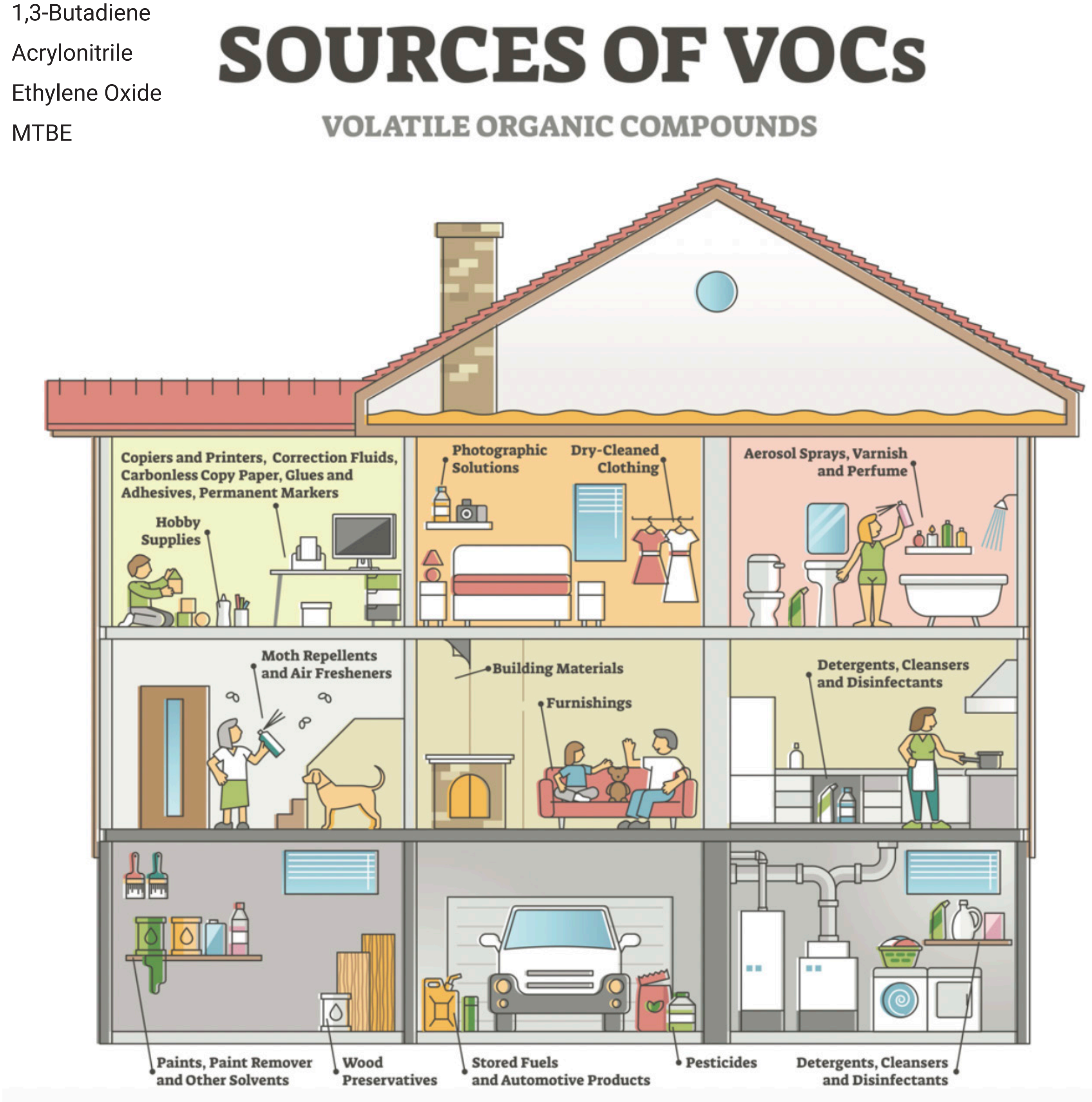
Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

VOLATILE ORGANIC COMPOUNDS

The EPA defines volatile organic compounds as a category of compounds that have a high vapor pressure and low water solubility. They are often synthetic chemicals used in the production of paints, pharmaceuticals, refrigerants, and other industrial products.

VOCs Tested:

- Xylene
- Styrene
- Benzene
- 1-Brompropane
- Propylene Oxide
- 1,3-Butadiene
- Acrylonitrile
- Ethylene Oxide
- MTBE



Volatile Organic Compound: Xylene

Markers Tested: 2MHA, 3MHA, 4MHA

CATEGORIZATION

Metabolite: 2-Methylhippuric Acid (2MHA), 3-Methylhippuric Acid (3MHA), 4-methylhippuric Acid (4MHA)

Parent Chemicals: Xylene

Category: VOC

GENERAL INFO

Xylene is an aromatic hydrocarbon that is used as a solvent in many industries. In terms of volume, is one of the top 30 chemicals produced in the United States[67]. Xylene naturally occurs in petroleum and coal tar and is often produced from petroleum.

EXPOSURE & SOURCES

- Used as a solvent in the printing, rubber, paint, and leather industries[67]
- Thinner for paint and varnishes, cleaning agents, rust preventives, shellac, synthetic fragrances, permanent markers, dry erase markers[67]
- Other sources include airplane fuel, gasoline, automobile exhaust, cigarette smoke, forest fires and industrial pollution[67]
- Soil and water contamination can occur from leaking underground storage tanks containing petroleum and contamination of groundwater can occur for several months before breaking down[67]
- Absorption: Mainly occurs from inhalation of xylene vapors and secondarily by oral intake via contaminated food and water or dermal absorption from contact with products high in xylene
  - Exercise can increase the amount of xylene absorbed[67]

PHYSIOLOGICAL EFFECTS

- Animal studies on xylene exposure have shown negative effects on many body systems including the CNS, liver, kidney, hemopoietic tissues and respiratory tract[68]

GENERAL CONSIDERATIONS

- Use low VOC paints when able
- Increase ventilation in areas using products with xylene
- Use protective gear when using products with xylene, such as gloves or a mask
- Use filtered water
- Avoid/limit heavy exercise near heavy traffic, as exercise can increase the amount of xylene absorbed by the lungs[69]
- Turn away and position yourself upwind from gasoline and car exhaust fumes

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** CYP2E1 is the main enzyme that breaks down xylene[70]
- **Phase 2:** Primary route is amino acid conjugation with glycine which then forms methylhippuric acid[69]
  - An alternate route includes glucuronidation, which may be an emergency mechanism when conjugation with glycine is not available[69]
- **Excretion:** Mainly occurs via the urine[71]
  - Most xylene leaves the body within 18 hours of exposure, however, 4-10% of xylene can be stored in body fat
  - Less than 5% is eliminated unchanged in exhaled breath[69]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: Styrene

Marker Tested: PGO (Phenylglyoxylic Acid)

CATEGORIZATION

Metabolite: Phenylglyoxylic Acid (PGO)

Parent Chemicals: Styrene

Category: VOC

GENERAL INFO

- PGO is a metabolite of styrene
- Styrene is a colorless liquid that is made from petroleum and natural gas to make materials such as latex and synthetic rubber[72]

EXPOSURE & SOURCES

- **Absorption:** Primarily occurs through inhalation as well as via the oral route
- **Inhalation:**
  - Pollution from companies manufacturing styrene
  - Automobile exhaust, cigarette smoke, use of photocopiers and laser printers[73]
  - Indoor air often has higher concentrations of styrene than outdoor air[73]
- **Orally:**
  - Consumption of food or water contaminated with styrene
  - Styrene can be found in groundwater, drinking water or soil samples[73]
  - Foods packaged in styrene-based products, such as plastic packaging, disposable cups & containers[72]
- **Other:**
  - Items made of polystyrene foam include surfboards, bean bags, flotation devices, etc.
  - Insulation for electrical wires & appliances, insulation for homes, fiberglass, plastic pipes, automobile parts, tires, carpet backing, children's car seats, appliances, toys[73]

PHYSIOLOGICAL EFFECTS

- Categorized as a possible carcinogen with IARC[73]
- Able to be passed through breast milk to infant[73]

GENERAL CONSIDERATIONS

- Limit/avoid styrene-based food packaging
- Avoid tobacco smoke (first and second hand)
- Limit exposure to car exhaust; Turn away and position yourself upwind from gasoline and car exhaust fumes
- Limit exposure to photocopiers or laser printers (or ensure room is aired out)
- Recommend using filtered water
- Recommend using an indoor air purifier

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Oxidation by CYP2E1 at low concentrations and CYP2B6 at high concentrations to form styrene 7,8-oxide. Styrene 7,8- oxide is then mainly metabolized by epoxide hydrolase to form styrene glycol and is subsequently converted to phenylglyoxylic acid (in addition to mandelic acid and hippuric acid)[73]
- **Phase 2:** An alternative pathway exists where styrene 7,8-oxide can undergo glutathione conjugation to form a different metabolite than PGO[73]
- **Excretion:** Urine is the main route of excretion for styrene
  - The half-life of urinary elimination of PGO is around 11 hours[73]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: Benzene

Marker Tested: NAP (N-acetyl phenyl cysteine)

CATEGORIZATION

Metabolite: N-acetyl phenyl cysteine (NAP)

Parent Chemicals: Benzene

Category: VOC

GENERAL INFO

- Benzene is a component of crude oil and found in gasoline as well as cigarette smoke

EXPOSURE & SOURCES

- **Absorption:** Mainly occurs through inhalation or oral exposure with minimal dermal absorption
- Natural sources of benzene include volcanoes and forest fires[74]
- Inhalation from benzene comes from emissions from burning coal and oil, benzene waste and storage operations, motor vehicle exhaust, cigarette smoke, electronic cigarettes[75], and evaporation from gasoline storage stations[76]
- Personal care products: It's typically not added as an ingredient but may be used in the manufacturing of body care products or via aerosol delivery
  - Sunscreen, hand sanitizers, deodorant, shampoo and conditioners, antifungal treatments

PHYSIOLOGICAL EFFECTS

- EPA, US DHHS, IARC all recognize benzene as a human carcinogen[77]
- Human studies show benzene exposure can increase development of acute myeloid leukemia (AML) and other leukemias[77]
  - The bone marrow is a major source of benzene toxicity[78]
- Benzene is distributed through the body rapidly and accumulates in fatty tissues[78]

GENERAL CONSIDERATIONS

- Limit/avoid exposure to cigarette smoke
- Limit/avoid exposure to car exhaust
  - Limit exercise on main roads exposed to car exhaust, such as biking behind cars, running, etc.
- Avoid standing near gas pump when refueling, instead stay in the car or stand away from the pump

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** CYP2E1 is the main enzyme catalyzing the oxidation reaction of benzene, and CYP2B1 and CYP2F2 to a lesser extent[79]
- **Phase 2:** Glutathione conjugation results in the formation of NAP (N-acetyl phenyl cysteine)[80]
  - Other pathways exist after phase 1 metabolism that result in the production of phenolic metabolites, which can undergo sulfation or glucuronidation, resulting in other urinary metabolites[78]
- **Other:**
  - Human study showed drinking green tea when exposed to benzene can decrease oxidative stress[80]
  - Genetic polymorphisms of CYP2E1, GSTs and mEH (microsomal epoxide hydrolase) enzymes can decrease the detoxification capacity of environmental toxins, such as benzene[81]
  - Broccoli sprouts: One human study found that a broccoli sprout beverage enhanced benzene detoxification when dosed appropriately[82]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: 1-Bromopropane

Marker Tested: NAPR (N-Acetyl Propyl Cysteine)

CATEGORIZATION

Metabolite: NAPR (N-Acetyl Propyl Cysteine)

Parent Chemicals: 1-Bromopropane (1-BP)

Category: VOC

GENERAL INFO

- 1-Bromopropane is a colorless liquid that's used as a solvent in many industries

EXPOSURE & SOURCES

- **Absorption:** Main ways of absorption include dermal contact or inhalation from products
- It is currently used as a solvent in adhesives, dry cleaning, vapor decreasing and electronic and metal cleaning industries[83]
- Specific applications include: degreasers, spot cleaner, stain remover, liquid spray/aerosol cleaner, adhesive sprays, sealants, mold cleaning, synthetic fiber manufacturing

PHYSIOLOGICAL EFFECTS

- The Department of Health & Human Services has classified 1-BP as "reasonably anticipated to be a human carcinogen"[84]
- Animal studies show 1-BP can result in reproductive organ toxicity and reduced sperm motility[85]
- 1-BP can also negatively affect the nervous system[84]

GENERAL CONSIDERATIONS

- Air out dry cleaning in a well-ventilated area for 24 hours before bringing it into the house or wearing it
- Opt for non-toxic dry cleaners

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** CYP2E1 is the main cytochrome P450 enzyme involved[84]
- **Phase 2:** Glutathione Conjugation; NAPR is formed from glutathione conjugation of 1-Bromopropane[86]
- **Elimination:** Urine is the main means of excretion
    - Half time in the urine is roughly 5-7.5 days[86]
    - Elimination of parent chemical can also occur via exhalation
- **Other:**
    - Melatonin may improve 1-NBP induced CNS toxicity by scavenging reactive oxygen species[87]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: Propylene Oxide

Marker Tested: NAHP (N-Acetyl (2,Hydroxypropl) Cysteine)

CATEGORIZATION

Metabolite: NAHP (N-Acetyl (2,Hydroxypropl) Cysteine)

Parent Chemicals: Propylene Oxide

Category: VOC

GENERAL INFO

- Propylene oxide is used in the production of polyethers (the main component of polyurethane foams) and propylene glycol[88]

EXPOSURE & SOURCES

- Propylene oxide is mainly used to produce propylene glycol, polyols for polyurethane foams and resins, functional fluids (hydraulic fluids, lubricants), propylene oxide-based surfactants, food fumigant, soil sterilizer and acid scavenger[89]
- Propylene glycol: Building materials, antifreeze, lubricants, electronic cigarettes, liquid, toothpaste, pharmaceuticals, cosmetics, artificial fog, preservative, food additive (food thickener, anti-caking agent, emulsifier, dough strengthener, moisture preserver, etc.)[90]
- Polyols: Polyurethane in car seats, mattress, and carpets, adhesives, paint
- Fumigation of foods and plastic medical instruments to reduce bacteria, mold, and yeast[89]
- Absorption: Occurs by ingestion from food or medications, inhalation, or dermal absorption

PHYSIOLOGICAL EFFECTS

- EPA has classified propylene oxide as a Group B2, probable human carcinogen[88]
- Animal studies show exposure can be carcinogenic, and have negative effects on reproduction, and development[88]

GENERAL CONSIDERATIONS

- Avoid foods and products containing propylene glycol and opt for alternative products without propylene glycol
- Limit exposure to new products with polyurethane material

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Inhibits CYP2E1[91]
- **Phase 2:** Glutathione Conjugation[92]
  - Another route of detoxification involves hydrolysis to propylene glycol via epoxide hydrolase[92]
- **Elimination:** Primarily occurs via urine, secondarily via exhalation of air

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: 1,3-Butadiene

Marker Tested: NADB (N-Acetyl (3,4-Dihydroxybutyl) Cysteine)

CATEGORIZATION

Metabolite: NADB (N-Acetyl (3,4-Dihydroxybutyl) Cysteine) (NADB)
Parent Chemicals: 1,3-Butadiene
Category: VOC

GENERAL INFO

1,3-butadiene is produced through processing petroleum and mainly used to produce synthetic rubber

EXPOSURE & SOURCES

- **Absorption:** Primarily comes from inhalation or via the oral route
- Occupational exposure: Synthetic elastomer (rubber and latex) production, petroleum refining, water treatment, agricultural fungicides, production of raw material for nylon, use of fossil fuels[93]
- Inhalation of automobile exhaust, pollution from industrial facilities, cigarette smoke[93]
- Foods that are contaminated from plastic or rubber containers

PHYSIOLOGICAL EFFECTS

- EPA has classified 1,3-butadiene as a known human carcinogen[93]
- Human epidemiological studies have shown increased risk of cardiovascular disease and cancer[93]
- Animal studies have shown a strong causal relationship with cancer, as well as reproductive and developmental problems[93]

GENERAL CONSIDERATIONS

- Limit exposure to first and second-hand tobacco smoke
- Limit heavy exercise in high traffic areas
- Use an air purifier as able

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** CYP2E1 is the main enzyme at low concentrations while CYP2A6 is the main enzyme at higher concentrations[94]
- **Phase 2:** Glutathione conjugation[95]
- **Elimination:** Primarily occurs via urine[94]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: Acrylonitrile

Marker Tested: NACE (N-Acetyl (2-cyanoethyl) Cysteine)

CATEGORIZATION

Metabolite: N-Acetyl (2-cyanoethyl) Cysteine (NACE)

Parent Chemicals: Acrylonitrile

Category: VOC

GENERAL INFO

Acrylonitrile is a synthetic chemical used to make plastics, acrylic fibers, and synthetic rubber[96]

EXPOSURE & SOURCES

- Absorption: The main route of absorption is via inhalation
- The main means of exposure is through occupational air exposure or individuals living near a factory producing acrylonitrile or a hazardous waste site[96]
- Small amounts may be found in water near industrial sites, but it is rapidly broken down in water and therefore does not commonly contaminate ground water[96]

PHYSIOLOGICAL EFFECTS

- EPA has classified acrylonitrile as a Group B1, probable human carcinogen[97]
- Animal studies indicate an increased incidence of tumors, decreased fertility and increased birth defects with acrylonitrile exposure[97]

GENERAL CONSIDERATIONS

- Limit exposure to industrial areas producing acrylonitrile

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Oxidation reaction mediated by CYP2E1 as the main enzyme involved in phase 1 detoxification[100]
- **Phase 2:** Glutathione conjugation. NACE is formed from glutathione conjugation of acrylonitrile[98]
- **Elimination:** Primarily excreted via urine
    - An animal study showed that after 10 days of acrylonitrile exposure, 61% was excreted in the urine, 3% in feces, 13% in exhaled air and 25% remained in the body covalently bound to tissues[99]
- **Other:** Acrylonitrile can be metabolized to cyanide following mostly dermal exposure[99]
    - An animal study showed that fasting may enhance CYP2E1 mediated oxidative metabolism of acrylonitrile and decrease liver glutathione levels, potentially increasing the toxicity of acrylonitrile exposure[100]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: Acrylonitrile, Ethylene Oxide

Marker Tested: HEMA (2-Hydroxyethyl Mercapturic Acid)

CATEGORIZATION

Metabolite: 2-Hydroxyethyl Mercapturic Acid (HEMA)
Parent Chemicals: Acrylonitrile, Ethylene Oxide
Category: VOC

GENERAL INFO

- HEMA is a urinary metabolite of several volatile organic compounds including acrylonitrile and ethylene oxide, both of which are found in cigarette smoke[101]

EXPOSURE & SOURCES

- Cigarette smoke is a major source of HEMA metabolite production
- Ethylene oxide is used as a chemical intermediate to make ethylene glycol (antifreeze), textiles, detergents, polyurethane foam, solvents, medicine, adhesives
- Ethylene oxide is used in smaller amounts as a fumigant for food (spices), cosmetics, and hospital sterilization

PHYSIOLOGICAL EFFECTS

- EPA has found ethylene oxide to be carcinogenic to humans by route of inhalation[102]
- Human occupational studies have shown increased cases of lymphoid and breast cancer with ethylene oxide exposure, while animal studies show lymphoid cancer and tumors in the brain, lung, connective tissue, uterus, and mammary glands[102]
    - Other negative effects are found with reproduction and development

GENERAL CONSIDERATIONS

- Avoid cigarette smoke, first and second hand

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Acrylonitrile is mainly metabolized by CYP2E1[103]
- **Phase 2:** Glutathione conjugation for acrylonitrile[103]
    - Acrylonitrile is metabolized by GSTP1, but not by GSTM1 or GSTT1 in humans[104]
- **Elimination:** Urinary excretion
- **Other:** Ethylene oxide is metabolized by nonenzymatic hydrolysis, enzymatic hydrolysis, and glutathione conjugation[105]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Volatile Organic Compound: MTBE

Marker Tested: 2HIB

CATEGORIZATION

Metabolite: 2-Hydroxyisobutyric Acid (2HIB)

Parent Chemicals: MTBE (Methyl-tertiary-butyl ether)

Category: VOC

GENERAL INFO

2HIB is a metabolite of MTBE. MTBE is a gasoline oxygenated compound that was used as an additive for unleaded gasoline in the US from the 1980s until 2005. MTBE increases vehicle octane ratings and helps to decrease pollution emissions[106]. Even though it's not currently used in the US as a gasoline additive, MTBE is still made in the US and exported to other countries

EXPOSURE & SOURCES

- Absorption: Inhalation, oral exposure and to a lesser extent dermal absorption
- When MTBE stopped being added to gasoline in 2005, environmental levels decreased significantly
  - If travelling, exposure can occur from other countries using MTBE
- Main sources of exposure include:
  - Contaminated water ingestion or dermal exposure; MTBE is capable of leaching into groundwater and can be slow to degrade in the environment[106]
  - Inhalation from contaminated ambient air
  - Living near a hazardous waste site
  - Occupational exposure with MTBE production[106]

PHYSIOLOGICAL EFFECTS

- Animal studies show high levels of inhalation can lead to decreased activity, reduced reflex and coordination, difficulty breathing, negative liver effects[107]
- Animal studies show high levels of ingestion can result in gastrointestinal irritation and damage or liver and male reproductive organs[107]

GENERAL CONSIDERATIONS

- Drink filtered water
- Contact the municipal water supply system to obtain information on MTBE levels in public water system, or test well water by a certified laboratory
- Children and adults should avoid playing near industrial or hazardous waste sites

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** CYP dependent demethylation to form tert-butanol and formaldehyde[108]; CYP2A6 is one of the main phase 1 detoxification enzymes involved in MTBE metabolism[109]
  - Additional oxidation reactions convert tert-butanol to 2HIB, the metabolite measured[108]
  - Increased metabolism to tert-butanol occurs with oral exposure compared to other routes of exposure[108]
- **Phase 2:** Glucuronidation; this process converts tert-butanol to a different glucuronide conjugate metabolite other than 2HIB[108]
- **Excretion:** Mainly excreted via urine
  - Animal studies showed urinary excretion at 36 hours post inhalation exposure was roughly 96-98%[108]

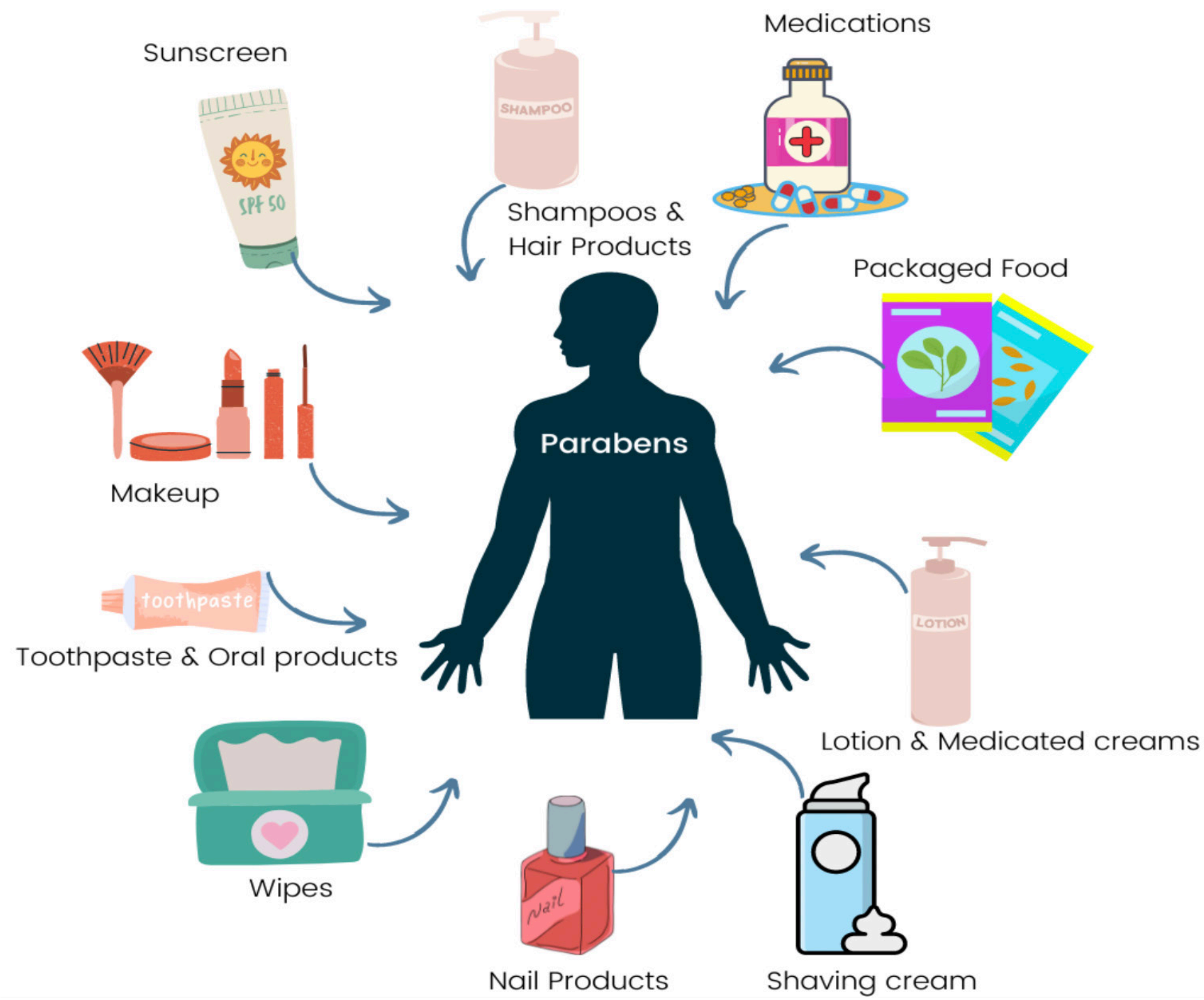
Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

PARABENS

Parabens are synthetic chemicals used as a preservative in many industries, such as cosmetic, pharmaceuticals, food, and beverage. Parabens are preferentially used in formulas because they don't have any odor or taste, they have a neutral pH, and they don't result in discoloring or hardening. Its antimicrobial activity is most effective against fungi and gram-positive bacteria.

Marker Tested:

- Methylparaben
- Propylparaben
- Butylparaben
- Ethylparaben



Parabens

Markers Tested: Methylparaben, Propylparaben, Butylparaben, Ethylparaben

CATEGORIZATION

Metabolite: ⊘
Parent Chemicals: Methylparaben, Propylparaben, Butylparaben, Ethylparaben
Category: Parabens

GENERAL INFO

- Estimated exposure is roughly 76mg per person per day, which is equal to roughly ½ cup per year of parabens[110]
- Females had significantly higher concentrations of methylparaben and propylparaben compared to males (likely due to body care product use)[110]
- According to the NHANES Study testing more than 2,548 participants, the CDC scientists found methylparaben and propylparaben in the urine of most people tested, indicating widespread exposure to these parabens

EXPOSURE & SOURCES

- Absorption: Occurs via dermal absorption and oral ingestion as the primary routes
- Even though parabens are low in food, absorption is greater from the GI tract than dermally[110]
- Body care products (dermal absorption): Women's cosmetics, shampoos, lipsticks & lipliners, mascara & eyeliner, sun-block, moisturizer, wipes, toothpaste, topical medicaments, hair care, shaving products[110]
- Pharmaceutical & OTC medications: Methylparaben, propylparaben and butylparaben are the 3 most common parabens found in medications[110]
- Foods: Mostly found in packaged foods
- Methylparaben & ethylparaben are the most common parabens in food. Propylparaben & butylparaben used to a lesser extent[110]
- Methylparabens found in pancake syrup, muffins, iced tea, pudding, turkey roast[110]
- Ethylparaben & propylparaben are commonly found in turkey breast, yogurt, apple pie & red wine[110]

PHYSIOLOGICAL EFFECTS

- In vitro and limited in vivo studies show that parabens have weak estrogenic activity, may induce growth of human breast cancer cells, and influence the expression of estrogen-dependent genes[114,111]
- In children, paraben exposure has been associated with increased prevalence of atopic dermatitis,[112] and some evidence of increased risk of asthma[113]

GENERAL CONSIDERATIONS

- Avoid body care products that contain parabens
- Consider limiting pharmaceutical medications containing parabens and determine if a compounding pharmacy can adjust formulation to eliminate parabens
- Limit intake of processed foods, which contain higher levels of parabens than whole foods

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Esterase Hydrolysis[114]
- **Phase 2:** Glucuronidation is the main phase 2 pathway, while sulfation and amino acid conjugation (with glycine) are also commonly used[114]
- **Excretion:** Urinary excretion is the predominant pathway[114]
  - Parabens are readily detected in breast milk and amniotic fluid
- Other: In vitro studies show ginger extract can inhibit paraben-induced hemolysis[115]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Parabens in Products

Product Type/Family	No. Containing Parabens	Total No. products	% Containing Parabens
Eye care products			
Makeup: eyeliners	33	33	42.9
Makeup: mascara	64	120	53.3
Makeup: eye shadow	6	33	18.2
Other makeups and ophthalmic products	4	112	3.6
Total	**107**	**342**	**31.3**
Facial products			
Makeup: face, powder	20	46	43.4
Makeup: face, other	25	48	52.1
Foundation	19	68	27.9
Other facial products Total	43	175	24.6
Total	**107**	**337**	**31.8**
Hair care products			
Hair care: shampoos	13	270	7.6
Conditioners	18	194	9.3
Hair care: dyes and dye kits	10	78	12.8
Hair care: stylers and treatments	38	290	13.1
Total	**79**	**832**	**9.5**
Lip products			
Lip liner	4	13	30.8
Gloss	4	26	15.4
Lipstick	5	43	11.6
Other lip balms and makeups	8	71	11.3
Total	**21**	**153**	**14**
Oral care products			
Toothpaste	1	76	1.3
Mouthwash/rinse	6	38	15.8
Oral, lip misc, other	3	12	25
Total	**13**	**138**	**9.4**
Nail care products			
Cuticle	5	12	41.7
Polish	3	21	14.3
Polish remover	1	6	16.7
Nail med, top/base coat, strengthener	4	36	11.1
Total	**13**	**75**	**17.3**
Miscellaneous oral products			
Perianal	10	16	62.5
Chewing gum	0	38	0
Otic Rx	0	5	0
Oral breath drops/mints/strips	0	12	0
Denture products	1	15	6.7
Total	**11**	**86**	**12.8**

Product Type/Family	No. Containing Parabens	Total No. products	% Containing Parabens
Household products			
Household products (not laundry)	2	160	1.3
Laundry detergents	1	82	1.2
Fabric softeners	0	41	0
Total	**3**	**283**	**1.1**
Medications, topical			
Acne/rosacea Rx	36	79	45.6
Acne/rosacea OTC	14	103	13.6
Anesthetic/pain relief/first aid OTC	22	62	35.5
Corticosteroid OTC	9	12	75
Corticosteroid brand Rx	18	92	19.6
Corticosteroid, generic, Rx	17	155	11
Antibiotic, Rx	6	16	37.5
Antibiotic, generic, selected, Rx	5	16	31.2
Medications: seborrhea Rx	4	6	66.7
Barrier products Rx	6	13	46.2
All other topical medicaments	35	199	17.6
Total	**172**	**753**	**22.8**
Skin care products			
Moisturizers	133	376	35.4
Antiaging/antiwrinkle/skin firming	75	191	39.3
Shaving	12	70	17.1
Soaps/cleansers	50	408	12.3
Antiperspirants/deodorants	3	163	1.8
Personal lubricant/fresheners	12	25	48
Sunscreens	37	201	18.4
All other skin care products	26	179	14.5
Total skin care	**348**	**1613**	**21.6**
Total camp products	**874**	**4621**	**19**

**Data obtained from The American Contact Dermatitis Society database of cosmetic and household products, known as the Contact Allergen Management Program (CAMP)[110]*

Parabens in Medications

Top Medications With Methylparaben	Top Medications With Propylparaben	Top Medications With Butylparaben
Acetaminophen 325 mg Acetaminophen/diphenhydramine 500 mg/12.5 mg	Acetaminophen 325 mg	Benadryl Allergy Kapgels diphenhydramine 25 mg
Benzonatate 100 mg Chlorpheniramine maleate extended-release 12 mg	Amantadine hydrochloride 100 mg	Chlordiazepoxide hydrochloride 10 mg
Chlorpromazine hydrochloride 100 mg	Anacin aspirin-free acetaminophen 500 mg Anafranil 25 mg	Diphenhist 25 mg
Cyclobenzaprine hydrochloride 10 mg	Benzonatate 100 mg	Diphenhydramine hydrochloride 25 mg
Disopyramide phosphate 100 mg	Benzonatate 100 mg	Diphenhydramine hydrochloride 25 mg
Docusate sodium 100 mg	Chlorpromazine hydrochloride 50 mg	Hydroxyurea 500 mg
Ergocalciferol 1.25 mg	Cyclobenzaprine hydrochloride 10 mg	Lescol 20 mg
Morphine sulfate SR 30 mg	Dexbrom. maleate/ Pseudoeph. ER 6 mg/120 mg Dipyridamole 75 mg	Loxapine succinate 25 mg
Morphine sulfate SR 15 mg	Disopyramide phosphate 100 mg	Loxapine succinate 5 mg
Nifedipine 10 mg	Docusate sodium 100 mg	Oxazepam 10 mg
Nortriptyline hydrochloride 25 mg	Ergocalciferol 1.25 mg	Phenytoin sodium extended 100 mg
Oxazepam 10 mg	Luoxetine hydrochloride 10 mg	Phrenilin forte acetamin. 650 mg/butalbital 50 mg
Tofranil-PM 75 mg	Methylergonovine maleate 0.2 mg	Seromycin 250 mg
Tofranil-PM 125 MG	Oxazepam 10 mg	Temazepam 30 mg
Valproic acid 250 mg	Tetracycline hydrochloride 250 mg	Temazepam 15 mg
Verapamil hydrochloride SR 120 mg	Verapamil hydrochloride SR 120 mg	Tetracycline hydrochloride 250 mg
Vimovo esomeprazole 20 mg/ naproxen 500 mg	Verelan 180 mg	Theophylline extended-release 200 mg
Zenatane 10 mg	Vimovo esomeprazole 20 mg/ naproxen 500	Theophylline extended-release 125 mg
		Theophylline extended-release 300 mg
		Tylenol extra strength 500 mg

**Data obtained from The American Contact Dermatitis Society database of cosmetic and household products, known as the Contact Allergen Management Program (CAMP)[110]*

- **Enteral and parenteral medications** that contain parabens include: multidose vial antibiotics, local anesthetics, corticosteroids, enteral and parenteral vitamins, diuretics, insulin, heparin, antihypertensives, chemotherapeutics agents, haloperidol and other syrups
- **Topical prescription** that contain parabens include: benzoyl peroxide, clindamycin, clocortolone, desonide, eflornithine, fluocinolone acetonide, fluorouracil, fluticasone, hydrocortisone, hydroquinone, imiquimod, metronidazole, salicylic acid, sertaconazole, sodium sulfacetamide, tretinoin and urea

Common Paraben Synonyms

Methylparaben

- Methyl paraben
- Methyl p-hydroxybenzoate
- Methyl 4-hydroxybenzoate
- Methyl parahydroxybenzoate
- n-Methyl-p-hydroxybenzoate
- p-Hydroxybenzoic acid methyl ester
- CAS 99-76-3
- Nipagin M
- Tegosept M
- Methyl parasept
- Benzoic acid, 4-hydroxy-methyl ester
- Maseptol
- Preserval M
- p-Oxybenzoesauremethylester
- p-Carbomethoxyphenol
- Methaben/methylben
- Metoxyde
- Preserval
- Metaben
- Moldex
- p-Methoxycarbonylphenol
- Paridol
- Septos
- Solbrol
- FEMA no. 2710
- Methyl butex
- Methyl Chemosept
- Solbrol M
- Abiol Aseptoform

Propylparaben

- Propyl paraben
- Propyl p-hydroxybenzoate
- Propyl 4-hydroxybenzoate
- Propyl parahydroxybenzoate
- n-Propyl p-hydroxybenzoate
- p-Hydroxybenzoic acid propyl ester
- CAS 94-13-3
- Nipasol M
- Tegosept P
- Propyl parasept
- Benzoic acid, 4-hydroxy-propyl ester
- Nipazol
- Propyl butex
- Betacide P
- Parasept
- Propagin Chemacide pk
- Chemocide pk
- Propyl parasept Aseptoform P
- Propyl chemosept
- Protaben P
- Betacine P
- Propyl aseptoform
- Nipagin P
- Nipasol P
- Solbrol P
- Bonomold OP
- Preserval P
- Paseptol

Ethylparaben

- Ethyl paraben
- Ethyl p-hydroxybenzoate
- Ethyl 4-hydroxybenzoate
- Ethyl parahydroxybenzoate
- Ethyl p-hydroxybenzoate
- p-Hydroxybenzoic acid ethyl est CAS 120-47-8
- Nipagin A
- Tegosept E
- Ethyl parasept
- Benzoic acid, 4-hydroxy-ethyl est
- Catalase
- Easeptol
- 1 ethyl butex
- HSDB 938
- Mycocten
- Nipagin A
- Nipazin A
- Solbrol A
- Sobrol A
- p-Carbethoxyphenol
- UNII-14255EXE39
- Aseptoform E
- Mekkings E
- Aseptin A
- Bonomold OE
- 3NSC 23514
- p-Oxybenzoesaeureaethylester
- Caswell no. 447
- Carbethoxyphenol

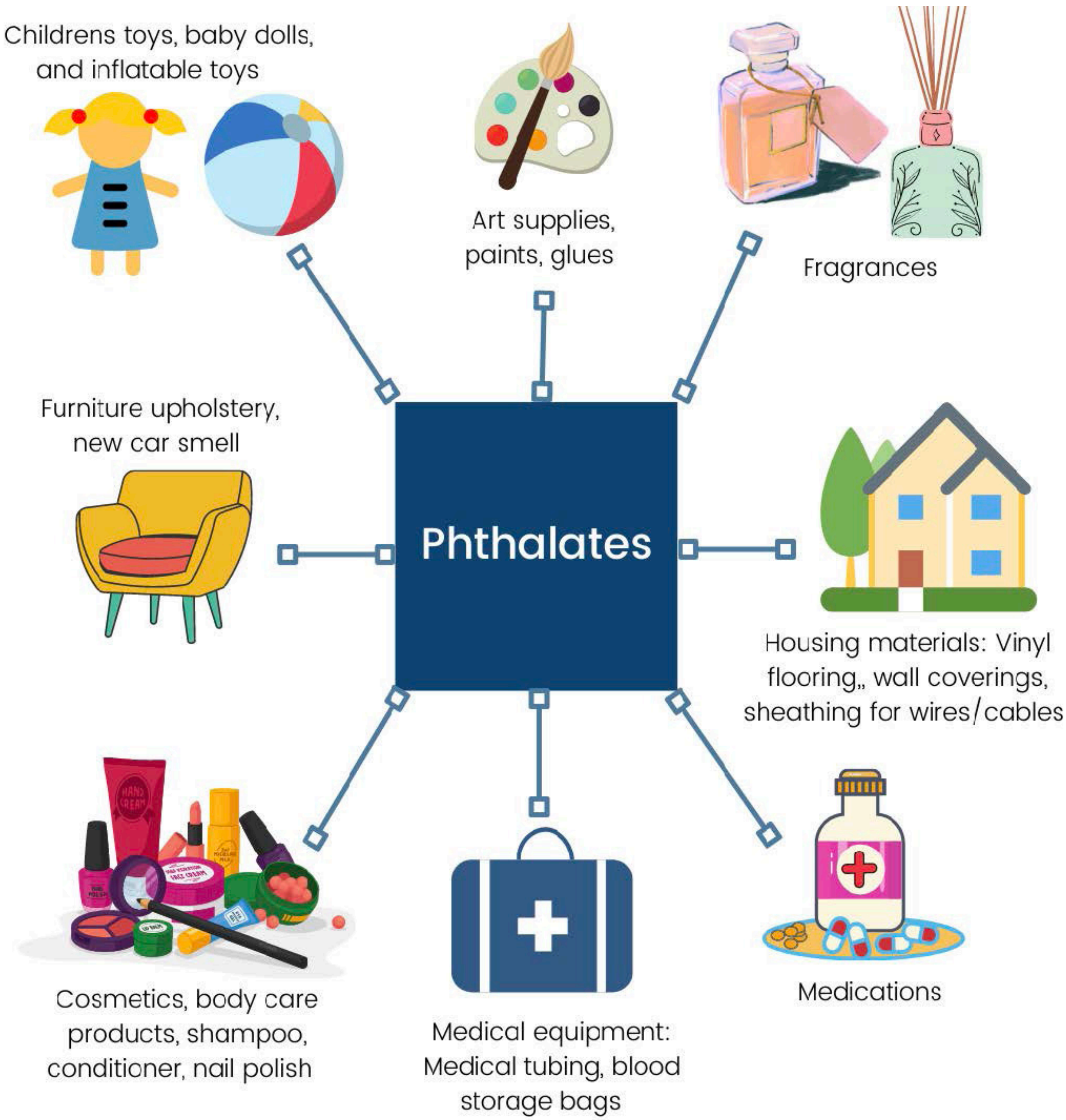
Butylparaben

- Butyl paraben
- Butyl p-hydroxybenzoate
- Butyl 4-hydroxybenzoate
- Butyl parahydroxybenzoate
- n-Butyl-p-hydroxybenzoate
- p-Hydroxybenzoic acid butyl ester
- CAS 94-26-8
- Nipabutyl
- Tegosept B
- Butyl parasept
- Benzoic acid, p-hydroxy-butyl ester
- Butyl chemosept
- Butoben
- Butyl tegosept
- Butyl butex
- Aseptoform butyl Preserval B
- Butyl parasept
- Solbrol B
- UNII-3QPI1U3FV8
- FEMA number 2203
- Caswell no. 130A
- 4-(Butoxycarbonyl)phenol Lexgard B
- n-Butyl-4-hydroxybenzoate FEMA no. 2203
- DSSTox_RID_75434
- Prestwick 0-3_000894
- EINECS 202-318-7
- EPA Pest. Chemical Code 061205

**Data obtained from The American Contact Dermatitis Society database of cosmetic and household products, known as the Contact Allergen Management Program (CAMP)*[110]

PHTHALATES

Phthalates are colorless, odorless, oily liquids that do not chemically bind to materials, allowing them to readily release from added products. They are categorized as a group of chemicals called plasticizers, which make plastic more flexible and durable. Phthalates is pronounced, THAL-ates. Phthalates have been labeled “The Everywhere Chemical” due to their ubiquitous nature in our daily lives.



Phthalates

Markers Tested: MEP, MEHP, MEOHP

CATEGORIZATION

Metabolite: Monoethyl Phthalate (MEP), Mono-2-ethylhexyl phthalate (MEHP), Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)

Parent Chemicals:

- MEP is a metabolite of diethyl phthalate (DEP)
- MEHP and MEOHP are metabolites of Di(2-ethylhexyl) Phthalate (DEHP)

Category: Phthalates

GENERAL INFO

- CDC researchers have found that phthalate exposure is widespread in the US[116]
- Adult women have higher levels of urinary metabolites compared to men, likely due to body care product use[116]

EXPOSURE & SOURCES

- **Absorption:** Occurs via dermal absorption predominantly, oral ingestion and some inhalation

Sources of phthalates:

- Personal care products such as soaps, shampoos, nail polish, fragrances, deodorant hair sprays, cosmetics[116]; DEP is the most common phthalate in these products because of the fragrance[117]
- Products made with polyvinyl chloride plastics (PVC): Wall coverings, tablecloths, vinyl flooring, furniture upholstery, shower curtains, garden hoses, pool liners, rainwear, baby dolls, inflatable toys, shoes, automobile upholstery, toothbrush, sheathing for wire/cables, medical tubing, blood storage bags[116,118]; DEHP is the most commonly used phthalate to make PVC products[117]
- Other sources: lubricating oils, insecticides, aspirin,[119] medical (blood transfusions, kidney dialysis, catheters, respirators)[120]
- Ingestion of contaminated foods due to migration of plastics from storage or processing or contaminated water[120]
- Hand to mouth behavior may increase exposure to phthalates, especially in children[116]
- Ambient air can contain higher phthalates, especially indoors with recent paint use or floor installation[120]

PHYSIOLOGICAL EFFECTS

- EPA categorizes DEHP as a possible human carcinogen[118]
- DEP and DEHP are listed in California's proposition 65 as a reproductive and developmental toxicant[117]
- Human studies have shown an increased risk of asthma in children through prenatal and direct phthalate exposure[121,122]
- Human studies demonstrate endocrine disrupting properties, contributing to increased breast cancer risk and male infertility[123]
- Animal studies of DEHP exposure show potential developmental toxicity, birth defects, decreased fertility, increased lung and liver weights from chronic inhalation, liver tumors[120]
- Babies in utero and infants can be highly susceptible due to phthalates readily detected in breast milk and amniotic fluid[124]

GENERAL CONSIDERATIONS

- Limit consuming foods from plastic packaging and limit microwaving plastic containers
- Avoid products that use the #3 in the universal recycling symbol, with the V or PVC listed[117]
- Opt for PVC and phthalate free products; Request phthalate free tubing and medical bags when necessary
- Limit hand-to-mouth contact with products containing phthalates
- Assess body care products for phthalates
- Consider an air purifier and water filter

DETOXIFICATION CONSIDERATIONS

- **Detoxification:** MEHP is formed from hydrolytic cleavage of DEHP by DEHP hydrolases; oxidation reactions predominantly by CYP2C91, CYP2C92 and CYP2C19 can convert MEPH to other metabolites such as MEOHP[125]
    - DEP undergoes hydrolysis to form the metabolite MEP[126]
- **Phase 2:** Glucuronidation[127]; glucuronide conjugates of MEHP and MEHP metabolites can also be formed and excreted[125]
- **Excretion:** Urine and feces are the main routes of excretion
    - Induce sweating to facilitate elimination of phthalates[128]
    - Estimated half-life of urinary elimination in humans is roughly 2-8 hours for DEHP[125]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

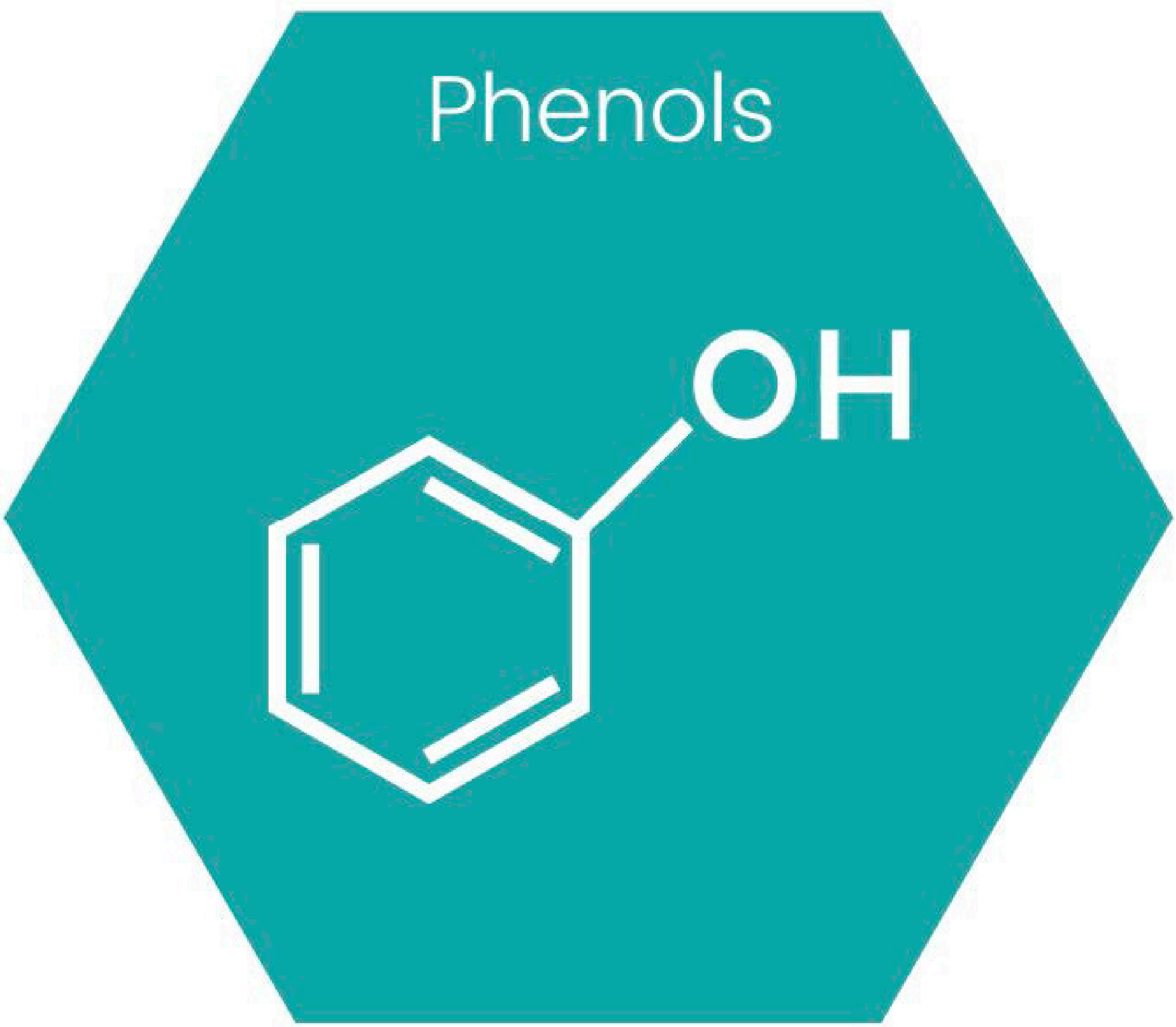
ENVIRONMENTAL PHENOLS

Phenols are a group of chemicals used ubiquitously in consumer and personal care products, food, and beverage processing and in pesticides. They are often used as preservatives in these products. They include the Environmental toxins listed below.

Marker Tested:

- Bisphenol A (BPA)
- Triclosan
- 4-Nonylphenol

Parabens are also considered environmental phenols, but they are listed in a separate category on this interpretive guide.



Environmental Phenol: BPA

Marker Tested: BPA (Bisphenol A)

CATEGORIZATION

Metabolite: ⊘

Parent Chemicals: Bisphenol A

Category: Environmental Phenol

GENERAL INFO

- Bisphenol A (BPA) is a chemical used in the production of polycarbonate plastics, epoxy resins and thermal paper[129]
- A study conducted by NHANES found that 93% of the urine samples tested from 2517 participants, showed detectable levels of BPA[130]

EXPOSURE & SOURCES

Sources:

- Products using BPA include baby bottles, water bottles, children's toys, nipples, food can lining, food packaging, food storage containers, eyewear, bottle tops, water supply pipes, medical equipment, sports safety equipment, electronic devices, CD/DVD discs, receipts, and dental sealants[130]
- Food contamination due to migration of plastics at each stage of food processing, leading to exponentially increased levels
- Increased migration of BPA can occur under conditions of decreased pH (more acidic), higher temperatures, & prolonged use
- BPA is used to make thermal paper and can be found in register receipts, books, faxes, and labels; recycled thermal paper can also be used to make brochures, tickets, envelopes, toilet paper, kitchen rolls, newspapers, and food cartons[130]

Absorption: Occurs mostly via ingestion, with smaller amounts through inhalation and dermal absorption

- Ingestion of BPA containing foods is a primary source of exposure
- Dust inhalation and dermal contact are a few other methods of exposure
- Medical procedures such as blood transfusions, kidney dialysis, catheter use, respirator use[130]

PHYSIOLOGICAL EFFECTS

- BPA is an endocrine disrupter, affecting function of sex hormones, leptin, insulin, and thyroxin[130]
- It is categorized as a xenoestrogen as it has estrogenic activity
- BPA also induces negative effects: hepatotoxic, immunotoxic, mutagenic, carcinogenic, decreased methylation, increased oxidative stress[130]
- Human exposure has also been associated with increased risk of obesity, diabetes, and heart disease[131]

PHYSIOLOGICAL EFFECTS

- Avoid microwaving polycarbonate plastic containers
- Limit packaged and processed foods
- Limit take-out food, especially hot and high fat foods, that are packaged in plastic take out containers
- Avoid products made with the recycle codes 3 or 7 since they can be made with BPA
- Decrease use of canned foods (only buy cans that specify BPA free)
- Use bottles that are labeled BPA free and use glass containers when possible
- Wash hands with soap and water after handling receipts
- *Note BPA free products may also be replaced with other potentially toxic ingredients/chemicals or other bisphenols (such as bisphenol S)

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Oxidation reactions can result in different metabolites; BPA may also act as an inducer of the CYP3A4 gene[132]
- **Phase 2:** Glucuronidation: BPA is metabolized by UDP-glucuonosyltransferase isoforms into its glucuronated form; sulfation is another conjugation reaction leading to BPA sulfate[133]
- **Excretion:** Feces is the main route of excretion, sweating is another means of elimination[134]
- **Other:** Interestingly, BPA can be degraded by different bacterial and fungal species in the environment. One study in fish found that probiotic administration decreases Bisphenol A induced reproductive toxicity[135]
    - Vitamin A: The extent of liver damage that occurs from BPA exposure is directly affected by retinoid levels. Consider a Micronutrient Test and/or or a NutriPro to assess for Vitamin A levels and genetic risk factors[136]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Environmental Phenol: Triclosan

Marker Tested: Triclosan

CATEGORIZATION

Metabolite: ⊘

Parent Chemicals: Triclosan

Category: Environmental Phenol

GENERAL INFO

- Triclosan (TCS) is an ingredient added to many products to control for bacteria
- In 2016 TCS was banned from soap products after a risk assessment conducted by the FDA; Triclosan is still found in high levels in other products[137]

EXPOSURE & SOURCES

- Personal care products: Toothpaste, mouthwash, hand sanitizer, surgical soaps[137]
- These products allow absorption dermally and through the oral mucosa
- Environmental exposure: Water and food contaminated with TCS
- Measurable levels are found in breast milk from nursing mothers[137]

PHYSIOLOGICAL EFFECTS

- TCS has been found to produce bacterial resistance; Bacteria found in the environment can also become resistant to TCS following exposure[137]
- Animal studies showed decreased variety of microbial species in the microbiome with TCS use[137]
- Exposure has been shown to induce mitochondrial uncoupling, act as an endocrine disruptor, impair reproduction and development, and may be carcinogenic[137]

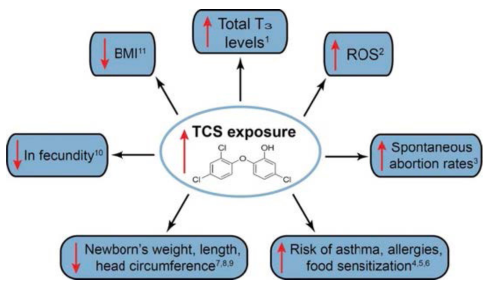


Image reference[137]

GENERAL CONSIDERATIONS

- Avoid products that use triclosan as an ingredient
- Special attention should be paid to hand sanitizers due to their ubiquitous use
- Use filtered water

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Hydroxylation reactions; 7 different CYP isoforms can metabolize triclosan, including CYP12A, CYP2B6, CYP2C19, CYP2D6, CYP1B1, CYP2C18, and CYP1A1[137]
- **Phase 2:** Glucuronidation and sulfation are the two main phase 2 detoxification pathways used[137]
  - TCS may also act as a metabolic inhibitor, where it can decrease activity of phase 2 enzymes involved in glucuronidation and sulfation[137]
- **Excretion:** TCS is primarily excreted via urine with the secondary route via fecal elimination[137]
  - TCS levels showed an average half-life of 21 hours; After roughly 8 days from exposure, TCS levels were similar to baseline levels[137]
  - The liver and adipose tissue showed the highest levels of TCS post exposure

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Environmental Phenol: 4-Nonylphenol

Marker Tested: 4-Nonylphenol

CATEGORIZATION

Metabolite: ⊘

Parent Chemicals: 4-Nonylphenol

Category: Environmental Phenol

GENERAL INFO

- Nonylphenols (NP) are nonionic surfactants or detergent like substances[138]
- 4-Nonylphenol is the most common commercial form of nonylphenol
- Nonylphenols are persistent in the aquatic environment and lead to bioaccumulation; they are also highly toxic to aquatic life[138]

EXPOSURE & SOURCES

- Used for a wide variety industries:
  - Industrial processes, consumer laundry detergents, personal hygiene, automotive, latex paints, lawn care products[138]
  - Contamination in soil, air, and all types of water can be a source of nonylphenol

PHYSIOLOGICAL EFFECTS

- May cause neurotoxicity, behavioral changes, and adverse effects on memory and learning[139]
- NP activates inflammatory cell signaling, particularly in the brain, and increases inflammatory cytokines
- Known endocrine disruptor that acts as a xenoestrogen[140]

GENERAL CONSIDERATIONS

- Use filtered water
- Avoid consuming seafood from water sources near wastewater treatment sites[141]

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** CYP1A2, CYP2B6, CYP1A1 show the highest activity for phase 1 detoxification[142]
- **Phase 2:** Glucuronidation[143] and sulfation[144]
- **Excretion:** Mainly via bile and fecal elimination
- **Other:**
  - Interestingly, NP can be degraded in the environment through the action of microorganisms. While studies have not looked at this, the health of the microbiome may be an important factor in oral exposure and degradation of nonylphenol[140]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Other Markers

Creatinine

Urine dilution and concentration can typically affect the level of analytes measured in the urine. To compensate for this, Vibrant uses a creatinine adjustment. This calculation divides the concentration of environmental toxins in the urine by the concentration of creatinine in the urine. This allows a very dilute or a very concentrated urine to appropriately adjust the levels of analytes in the urine.

Other Marker Tested:

- Tiglyglycine: Mitochondrial Marker
- DPP: Aryl Phosphates
- NAE: Acrylamide
- Perchlorate

Mitochondrial Marker

Marker Tested: Tiglyglycine

CATEGORIZATION

Metabolite: ∅
Parent Chemicals: ∅
Category: Other Markers/ Mitochondrial Marker

GENERAL INFO

- Mitochondria are essential for ATP synthesis to meet cellular energy demands. They also serve other functions in the body such as, apoptosis, generation and detoxification of reactive oxygen species, intracellular calcium regulation, steroid hormone and heme synthesis and lipid metabolism. Evidence exists showing that environmental exposures can contribute to significant mitochondrial dysfunction. Several diseases and conditions are associated with mitochondrial dysfunction, therefore providing a potential link between environmental toxins and certain disease states[145]
- TG is used as a diagnostic marker in disorders of the respiratory chain[146]
  - NAD+ is produced from complex I of the electron transport chain (ETC). When NAD+ is insufficient due to impairments in the ETC, it can lead to buildup of tiglyglycine levels. This occurs because 2-methyl-3-hydroxybutyryl-CoA dehydrogenase requires NAD+ as a cofactor
  - TG is formed from Tiglyl CoA, an intermediate of isoleucine metabolism, by the action of glycine-N-acyltransferase
- Various environmental toxins have been shown to inhibit complex 1 of the ETC, which can result in elevated levels of tiglyglycine
- Elevated levels can also be seen with: Beta-ketothiolase deficiency, 2- MAA thiolase deficiency, propionyl CoA carboxylase deficiency, Pearson syndrome, methylmalonic acidemia and other disorders of the respiratory chain[146]

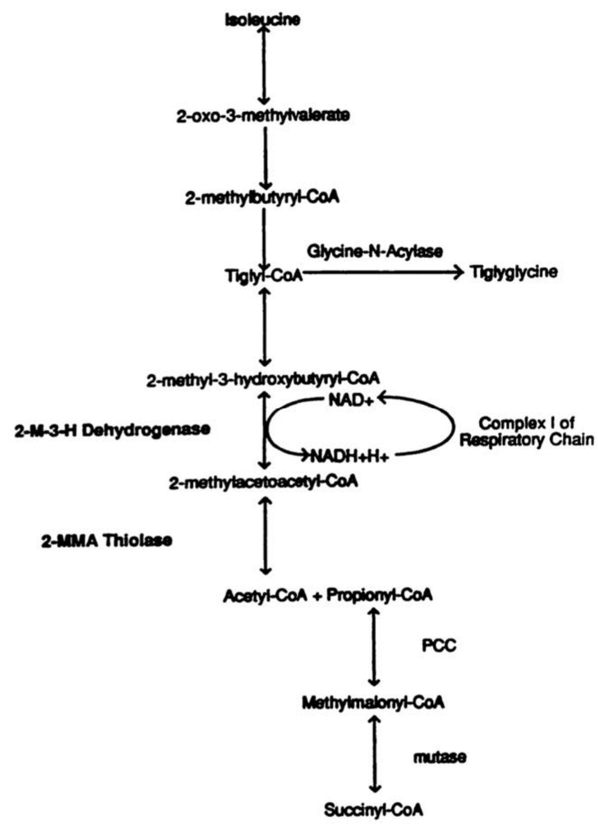


Image reference[146]

GENERAL CONSIDERATIONS

- Remove exposure to environmental toxins that may be contributing to impaired mitochondrial function
- Support mitochondrial function with diet and nutraceuticals for Complex I support[147]:
  - Fatty acids
  - Carnitine
  - Antioxidants
  - Folate (in some cases)
- NAD+ supplementation to provide cofactor support for 2-M-3-H Dehydrogenase enzyme[146]

Other Marker: Aryl Phosphates

Marker Tested: DPP (Diphenyl Phosphate)

CATEGORIZATION

Metabolite: Diphenyl Phosphate (DPP)

Parent Chemicals: Aryl phosphates:

- Triphenyl phosphate (TPP)
- 2-ethylhexyl diphenyl phosphate (EHDP)
- Resorcinol bis (diphenylphosphate) (RDP)[148]

Category: Other

GENERAL INFO

- Aryl phosphates are used in many industries such as in flame retardants, plasticizers, lubricants, hydraulic fluids, and oxidizers[148]; Some common aryl phosphates include TPP and EHDP
- As other flame retardants have been phased out, such as PBDEs, there has been increased use of organophosphate flame retardants, such as TPP[149]

EXPOSURE & SOURCES

- **Absorption:** Inhalation of vapors or particulates released from materials containing flame retardants is a main source of absorption; Dust can also act as a continuous source of exposure[150]; Oral ingestion from food and water
- **EHDP** is mostly used in flexible PVC as a plasticizer and a flame retardant; It is also used in polyurethanes, rubber, paints, textile coatings, photograph film, adhesives, and food packaging applications; food products in various countries can also contain EHDP
- **TPP** is commonly used as an additive flame retardant in household products such as upholstered furniture, mattresses, children's products, motor vehicle seats, some car seats, carpet padding, electronic equipment; TPP is also found in nail polish/ products as a plasticizer
- **Food or water:**
    - Aryl phosphates contaminate soil and groundwater systems especially near industrial sites[148]
    - Meat and fish intake were associated with higher DPP levels, while increased dairy & fresh foods were associated with lower DPP levels[149]
- **Other:** Hydraulic fracturing related spills, also known as "fracking" can introduce DPP into the environment[148]

PHYSIOLOGICAL EFFECTS

- Organophosphate flame retardants have been linked to reproductive and endocrine changes in humans
- Studies on TPP in human cell lines have demonstrated carcinogenic effects as well as damage to immunologic, neurologic, and developmental systems[149]
- TPP can induce obesogenic activity in human cells & disrupt cardiac development in non-human vertebrates[149]

GENERAL CONSIDERATIONS

- Opt for household products without organophosphate flame retardants. Furniture labels containing "TB117" are more likely to contain flame retardants[149]
- Replace upholstered furniture that is torn or has crumbling foam[149]
- Clean, dust and mop often a damp cloth/mop
- Use a HEPA vacuum cleaner
- Consider an air purifier
- Limit/avoid use of nail polish (even natural and eco-friendly options can contain TPP)

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Hydrolysis of triphenyl phosphate forms diphenyl phosphate[151]
- **Phase 2:** Animal studies showed glutathione conjugation is an important phase 2 pathway for TPP metabolism[151]
- **Excretion:** Urine; Animal studies showed EHDP is primarily excreted via urine with roughly 80% excreted within the first 24 hours from oral exposure[152]; biliary excretion for EHDP is low

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Other Marker: Acrylamide

Marker Tested: NAE (N-Acetyl-S-(2-carbamoylethyl)-cysteine

CATEGORIZATION

Metabolite: N-Acetyl-S-(2-carbamoylethyl)-cysteine (NAE)

Parent Chemicals: Acrylamide (AA)

Category: Other

GENERAL INFO

- Acrylamides (AA) are formed from the Maillard reaction between sugars from carbohydrates and amino acids (particularly asparagine) when they are cooked at very high temperatures, such as frying, roasting and baking[153]
- According to the Fourth Report on Human Exposure to Environmental Chemicals, CDC found measurable levels of acrylamide in 99.9% of the US population[154]

EXPOSURE & SOURCES

- **Absorption:** AA is most commonly absorbed through ingestion and inhalation
- **Food:** AA is found at higher concentrations in high temperature cooked potato, grains, and coffee products; this includes French fries, potato chips, baked goods, cereals, crackers, breads (especially the crust), biscuits, chocolate[155,162]
  - Other foods such as dairy, meat and fish do not typically form high levels of AA
- **Smoking:** Cigarette smokers had twice the level of AA in their body compared to nonsmokers[156] and electronic cigarettes users also show higher levels of AA[157]
- **Monomeric acrylamide** is a synthetic industrial chemical used to produce polymers & copolymers[158]
  - Polyacrylamide is commonly used in sewage and wastewater treatment plants, treatment of potable water, the paper industry to strengthen paper quality, a petroleum additive & gels for electrophoresis[158]
  - Acrylamide monomer is used for grout production, soil stabilizers, dam construction, foundations, tunnels, roadways & lesser utilization in photography, adhesives & textile industries[158]

PHYSIOLOGICAL EFFECTS

- AA is categorized as a 2A carcinogen (carcinogenic potential in humans)[162]
- AA is rapidly distributed to all organs, including the brain, heart, liver, kidneys, and breast milk[162]
- AA is able to accumulate & persist in RBC's; It is thought to react with sulfhydryl groups found in hemoglobin[158]
- AA has been shown to bind to nucleic acids & proteins in vivo, & DNA in vitro; the adduct formation may be the pathogenesis of toxicity associated with AA[158]
- Animal studies show AA can be genotoxic, carcinogenic, and neurotoxic effects with negative effects on male reproductive system and on pre and post development[162]
- The neurotoxic effects of AA in humans also extend to sensory and motor neuropathy, drowsiness and cerebellar ataxia[159]

GENERAL CONSIDERATIONS

- See next page for tips on how to reduce acrylamide production when cooking
- Avoid exposure to cigarette smoke, both firsthand and secondhand

DETOXIFICATION CONSIDERATIONS

- **Phase 1:** Cytochrome P450 (CYP2E1)[160]
- **Phase 2:** Glutathione Conjugation[158]
  - AA is predominantly metabolized by glutathione conjugation to form the main metabolite, NAE
  - Glutathione precursors such as NAC and methionine have been shown to protect against the cytotoxicity of AA and other metabolites[161]
- **Excretion:** Urine; AA is rapidly metabolized, with over 60% excreted in the urine within 24 hours[161]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways

Reduce Acrylamide Levels

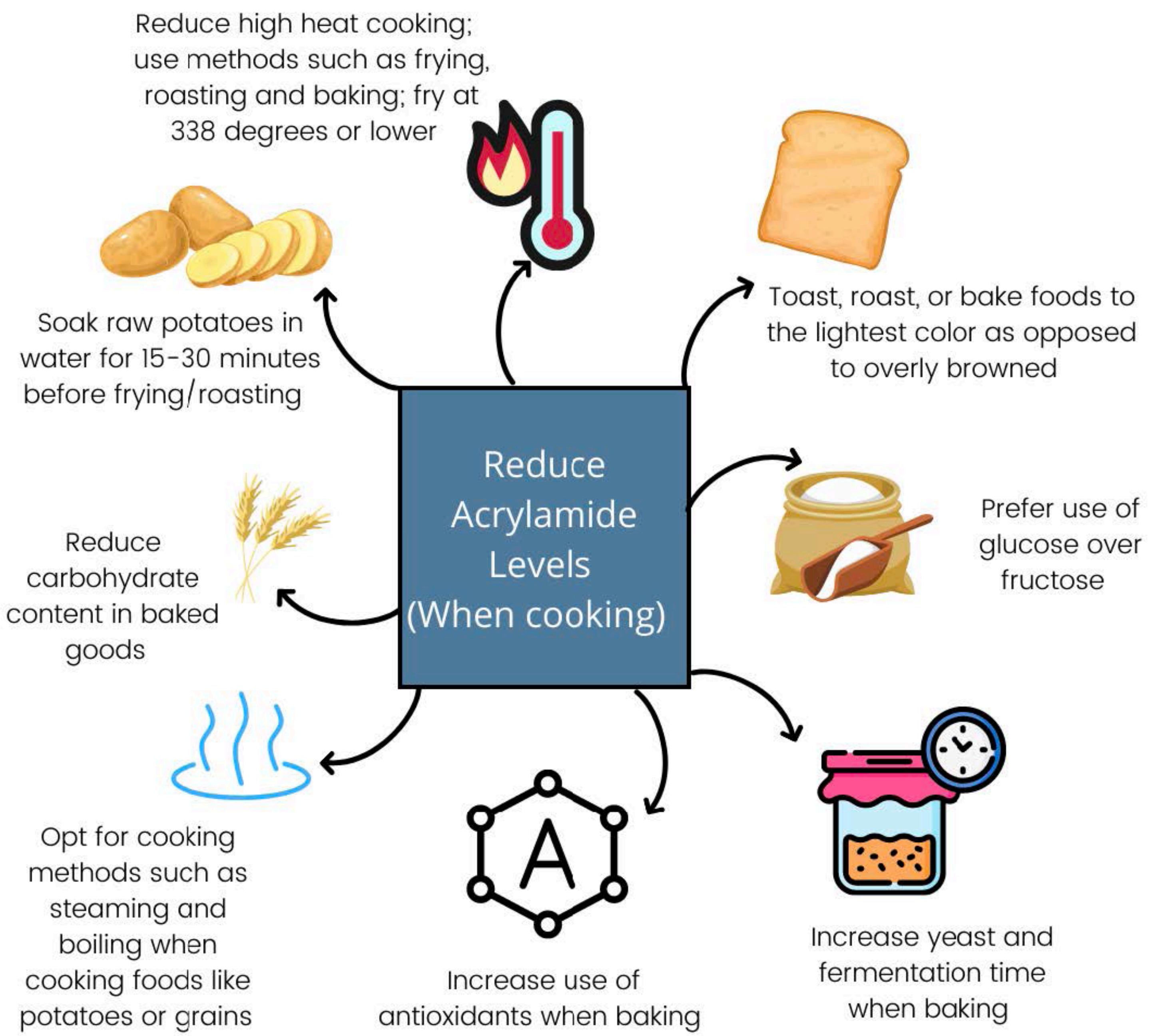


Image reference[162]

Other Marker: Perchlorate

Marker Tested: Perchlorate

CATEGORIZATION

Metabolite: ⊘

Parent Chemicals: Perchlorate

Category: Other

GENERAL INFO

- Perchlorates refer to inorganic compounds that contain a perchlorate anion bonded to a positively charged group (ammonium, alkali, or alkaline earth metal)[163]
- According to the *Fourth Report on Human Exposure to Environmental Chemicals*, CDC scientists found perchlorate in all 2,504 participants tested in the US[164]

GENERAL INFO

- Perchlorate occurs naturally in arid states in the Southwest U.S. (Texas, New Mexico), nitrate fertilizer deposits in Chile and potash ore (potassium salt deposits buried over geologic time) in the US and Canada[165]
- Perchlorate can also form naturally form in the atmosphere
  - This may contribute to elevated levels in water and food sources
- Perchlorate is also manufactured as an industrial chemical for use in rocket propellant, explosives, fireworks, gunpowder, and road flares[165]
- Contaminated water: Occurs near natural sources, in other areas due to atmospheric levels contaminating rainfall & areas near manufactured, disposal or release of perchlorate. It can affect groundwater wells, lakes, rivers, rainfall
  - Contaminated water can affect drinking water, produce grown with contaminated water, such as leafy green vegetables and animal accessing contaminated water affecting products such as milk
- Other sources: low levels can also be found in products such as bleach and tobacco products
- Exposure can also occur through breast milk
- **Absorption:** One of the main routes of absorption is orally through ingestion of contaminated water or foods, while dermal absorption is expected to be negligible

PHYSIOLOGICAL EFFECTS

- Exposure to perchlorate in humans can interfere with iodide uptake in the thyroid gland potentially contributing to impaired thyroid function and hypothyroidism[165]

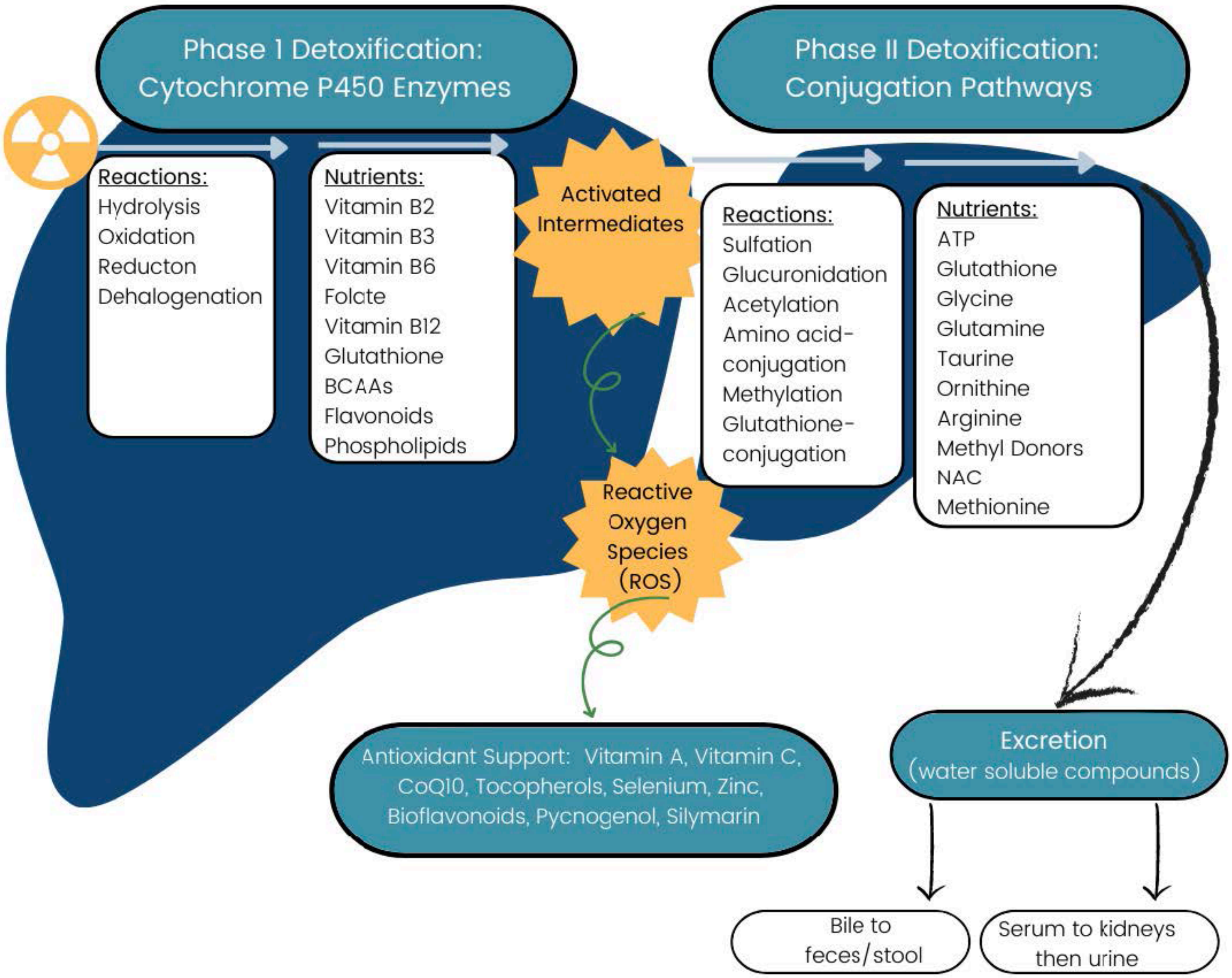
PHYSIOLOGICAL EFFECTS

- Consider water filtration for drinking water and bathing
- Caution consuming produce or animal products (milk), in areas of high natural or manufactured perchlorate
- Avoid/limit nitrite fertilizer from Chile
- Consider increasing iodine rich foods and consider supplementation if levels are low[166]
- Testing Considerations: Thyroid Panel, Serum Iodine

DETOXIFICATION CONSIDERATIONS

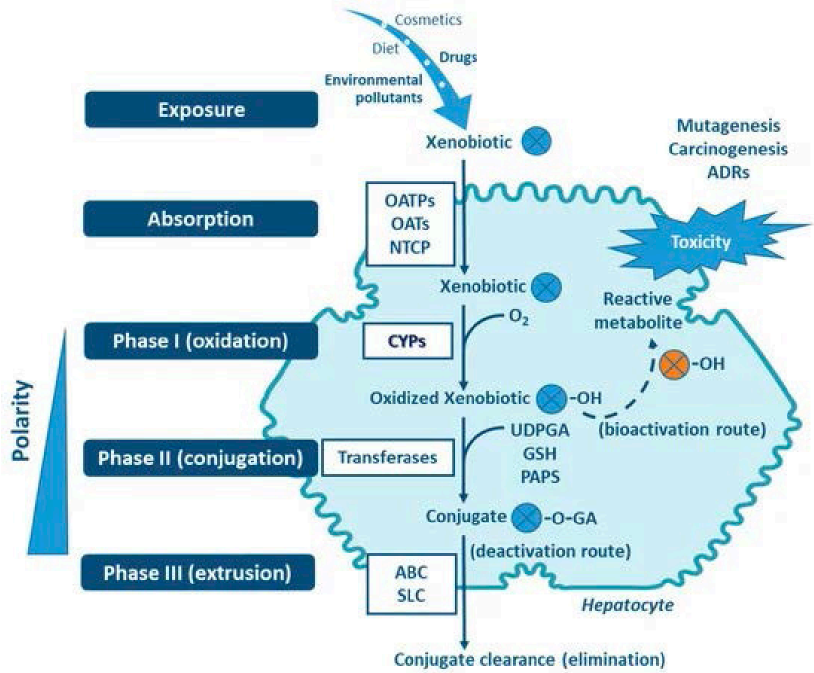
- **Detoxification:** Perchlorate is excreted as is, with little metabolic change.
- **Excretion:** Perchlorate is readily excreted in the urine
  - It has a half-life of approximately 8-12 hours[167]

Please see recommendations at the end of the interpretive guide to support and upregulate corresponding detoxification & excretion pathways


Phase 1 Detoxification:
Cytochrome P450 Enzymes
Reactions:
Hydrolysis
Oxidation
Reducton
Dehalogenation
Nutrients:
Vitamin B2
Vitamin B3
Vitamin B6
Folate
Vitamin B12
Glutathione
BCAAs
Flavonoids
Phospholipids
Activated Intermediates
Reactive Oxygen Species (ROS)
Phase II Detoxification:
Conjugation Pathways
Reactions:
Sulfation
Glucuronidation
Acetylation
Amino acid-conjugation
Methylation
Glutathione-conjugation
Nutrients:
ATP
Glutathione
Glycine
Glutamine
Taurine
Ornithine
Arginine
Methyl Donors
NAC
Methionine
Antioxidant Support: Vitamin A, Vitamin C, CoQ10, Tocopherols, Selenium, Zinc, Bioflavonoids, Pycnogenol, Silymarin
Excretion
(water soluble compounds)
Bile to feces/stool
Serum to kidneys then urine

OVERVIEW OF DETOXIFICATION PHASES & ELIMINATION

Image reference[168]



1

PHASE 1 DETOXIFICATION

Functionalization- Adds a reactive site to the lipid soluble toxic compound. Uses the Cytochrome P450 enzyme system and other enzymes involving a variety of reactions (hydrolysis, oxidation, reduction, etc.).

2

PHASE 2 DETOXIFICATION

Conjugation- Adds a water-soluble group to the reactive site formed from phase 1 to make the toxin more water soluble and to prepare it for excretion.

3

PHASE 3 DETOXIFICATION

The anti-porter system is a transport system that moves conjugated metabolites formed from phase 2 detoxification out of cells and also plays a role in efflux of toxins prebiotransformation

4

EXCRETION

Eliminates the toxin out of the body:

- Bile to stools
- Kidney to urine
- Exhalation from lungs
- Skin through sweat

SUPPORT EXCRETION

GENERAL INFO

Toxins are excreted through multiple pathways in the body. It's important to optimize elimination pathways prior to initiating a detoxification program to ensure proper removal of toxins from the body. If excretion is compromised, there can be a buildup of toxins in the body that can lead to negative health effects. The main routes of elimination include urine, fecal, exhalation and sweat. To a lesser extent, toxins can also be excreted via breastmilk.

KIDNEYS-> URINE

Excretion of toxin through the kidneys and into the urine is one of the most important routes of elimination. When toxins are filtered through the glomerulus in the kidney, they undergo exchange along the tubular segment to either be partially reabsorbed into the blood or excreted in the urine. One factor that affects reabsorption is the pH of the urine. Electrically neutral molecules are subject to reabsorption from urine into blood by sample passive diffusion. Lipophilic substances are typically reabsorbed at higher rates from the tubules compared to hydrophilic substances. In a state of moderate alkaline urine, weak organic acids are present mainly as ionized or electrically charged molecules and this prevents their diffusion from urine back into blood and promotes their elimination through urine. When the urine is more acidic, weak acids such as glucuronide and sulfate conjugates are less ionized increasing the likelihood of reabsorption and decreasing the rate of urinary excretion. On the contrary, acidic urine pH may increase the excretion of bases. Impaired kidney function, induced from toxicant damage, infections, or aging results in decreased ability to remove toxins and increased likelihood of reabsorption.

BILE-> FECES

Many toxins are excreted in bile, which then enters the intestines for elimination from the body. There is also the possibility that toxins in the intestines can be reabsorbed back into the system via enterophepatic circulation. Often this occurs due to enzymes present in the gut, like beta-glucuronidase, which hydrolyzes glucuronide conjugates, increasing their likelihood of reabsorption. When this happens, it can prolong the exposure of toxins in the body and potentially lead to exposure of a more toxic form than the originally excreted toxin. In order to counteract this effect, there are a few recommendations such as incorporating binders to bind to the toxin for more effective removal from the body and assess/address elevated beta-glucuronidase levels in the gut. It's also critical to ensure that constipation does not occur, which can increase the chances of toxin reabsorption.

SKIN -> SWEAT

Sweat is a recognized excretory route for various environmental toxins and heavy metals. Specific environmental toxins, such as BPA have been studied and sauna therapy has shown to increase excretion of BPA through sweating. Other studies have shown that heavy metals, medications, and other toxins can be readily excreted through the skin. There are also many studies that demonstrate physiological benefits from sweating therapy, such as improved cardiovascular function, respiratory function, pain severity in fibromyalgia patients, metabolic dysfunction, diabetes, and obesity to name a few[169].

EXHALATION

Exhaled air is another route of excretion for various compounds. While this guide will not go into detail about supporting exhalation, there may be some generous considerations to consider, such as limiting exposure to air pollution, focusing on deep breathing, and opting for air purification methods when able.

Elimination Considerations

	DIET CONSIDERATIONS	LIFESTYLE CONSIDERATIONS	SUPPLEMENT CONSIDERATIONS	TESTING CONSIDERATIONS
KIDNEYS-> URINE	• **Consume adequate (filtered) water** • A high protein diet may increase the acidity of the urine and potentially increase the reabsorption of certain toxins[170] • **Increase potassium rich foods** to promote urine alkalinization: potato, prunes, raisins, lima beans, banana, acorn squash, tomato juice[170] • A pilot trial found 200g cooked broccoli, carrots & cauliflower increased urine alkalinization for up to 4 hours afterwards[170]	**Exercise:** Affects renal excretion by increasing urinary pH which neutralizes weakly basic drugs and limiting their excretion, while increasing excretion of acidic drugs[171]	**Citrate compounded minerals[172]:** to increase alkalinization of urine • Magnesium Citrate • Potassium citrate • Zinc citrate • Calcium citrate	**Kidney function panel** **Urinalysis**
BILE-> FECES	• **Increase fiber intake:** to promote bowel movements • **Increase intake of healthy fats:** Healthy fats increase the production of bile that can assist in detoxification • **Increase polyphenol rich foods** (adsorb bile acids): apples, grapes, red beets, asparagus roots, persimmon[173]	**Exercise:** Increases bile acid flow and excretion, while decreasing intestinal reabsorption[171]; may also improve bowel movements	**Increase Bile:** • **TUDCA**[174] (Tauroursodeoxycholic acid): (animal study showed 250% increase in bile) • **Artichoke Extract:** 1.92g[175] **Binders** (adsorb bile): • **Activated charcoal**[176] • **Zeolites**[177] **Improve Constipation:** • **Magnesium oxide[178]:** .5g TID • **Probiotics**[179] **Other:** • **EGCG:** increase fecal bile acid excretion (animal)[180]	**Gut Zoomer:** To assess for beta-glucuronidase levels
SWEATING	• **Increase electrolytes:** Consider foods and drinks that contain adequate electrolytes; • Note: While sweating increases electrolyte loss (sodium, potassium, chlorine) through the skin, the body can compensate by hormonal regulation via increased aldosterone production from the adrenal glands[181]	**Exercise:** Increases sweating for increased depuration (removal of impurities from the body)[182] **Sauna[182]:** Increases sweating for increased depuration; multiple established protocols that include sauna therapy: the Hubbard Method, Crinnion Cleansing Program, Dr. Rea protocols, Waon Therapy[169]	**Electrolyte replacement:** Sodium and potassium replacement **Diaphoretic Herbs** (promote sweat coming out of skin pores): Garlic, nettle, wormwood, German chamomile, pennyroyal, sweet basil, feverfew, anise, Egyptian clover[169]	**Comprehensive Metabolic Panel (CMP)** **Micronutrient:** to assess mineral and electrolyte levels

SUPPORT PHASE 2 DETOXIFICATION

PHASE 2 DETOXIFICATION:

This is the second phase of detoxification, also known as conjugation. This step involves adding a water-soluble group to the reactive site formed during phase 1 detoxification. The process of conjugation, or transferring a hydrophilic compound, is categorized into different types of pathways depending on the compound/enzymes used. The purpose of these phase 2 reactions is to make the metabolite more hydrophilic and less toxic to improve excretion out of the body. The primary site of biotransforming enzymes is the liver, with the kidneys and lungs making up 10-30% of the livers capacity and the smallest concentrations found in the skin, intestines, testes, and placenta. There are also many factors that can influence the activity of biotransformation, which include genetics SNPs, diet, nutrient deficiencies, supplements and medications, disease states, age, gender, dose of toxins and exposure to toxins.

- **Glucuronidation:** Involves transferring glucuronic acid (hydrophilic compound) to the reactive site formed from phase 1, via glucuronyl transferases
- **Glutathione Conjugation:** Involves transferring glutathione (hydrophilic compound) to the reactive site formed from phase 1, via glutathione transferases
- **Sulfation:** Involves transferring sulfate (hydrophilic compound) to the reactive site formed from phase 1, via sulfotransferases
- **Acetylation:** Involves transferring acetyl groups (hydrophilic compound) to the reactive site formed from phase 1, via N-acetyl transferases
- **Amino Acid Conjugation:** Involves transferring amino acids (hydrophilic compound) to the reactive site formed from phase 1, via amino acid transferases
- **Methylation:** Involves transferring a methyl group (hydrophilic compound) to the reactive site formed from phase 1, via N- and O-methyltransferases

Phase 2 Detoxification Considerations

	Diet Considerations	Supplement Considerations	Testing Considerations
Glutathione Conjugation	**INDUCERS**[183] • Vegetables: Cruciferous, allium vegetables • Resveratrol foods: Grapes, wine, peanuts, soy, itadori tea • Ellagic acid foods: Berries, pomegranate, grapes, walnuts, blackcurrants • Genistein: Soy, miso, tempeh • Tea: Green tea, rooibos tea, honeybush tea • Other: Rosemary, ghee, purple sweet potato, fish oil, black soybean, citrus **INHIBITORS**[183] • Quercetin: Apple, apricot, blueberries, yellow onion, kale, alfalfa sprouts, green beans, broccoli, black tea, and chili powder • Genistein: Fermented soy, miso, tempeh **OTHER:** • Whey protein (^{40}/d) has been shown to increase glutathione levels[184]	• **Glutathione (liposomal or oral):** 500-1000 md/d[184] *Other forms may also be used such as IV, transdermal, intranasal • **N-Acetyl Cysteine** (Rate limiting precursor for GSH synthesis): 600-1200mg/d (divided doses)[184] • **Glycine** (Precursor for GSH synthesis): 100mg/kg/d[184] • **Selenium** (Supports glutathione peroxidase): 100-200ug/d[184] • **Alpha lipoic acid** (Support glutathione reductase): 200-600mg/d[184] • **B Vitamins:** B2 (supports glutathione reductase), B5, B12[184] • **Vitamin C:** 500-100mg/d[184] • **Vitamin E:** 100-400IU/d[184] • **Omega 3 fatty acids:** 4g/d[184] • **Pycnogenol**[185]**:** 1mg/kg/day decreased oxidized GSH & increased reduced GSH • **Curcumin**[184]	**Micronutrient:** To assess glutathione levels **NutriPro:** To assess genetics related to glutathione **Organic Acid test:** To assess indirect markers for glutathione status **Gut Zoomer:** To assess for optimal protein digestion
Glucuronidation	**INDUCERS**[183] • Cruciferous vegetables • Resveratrol foods: Grapes, wine, peanuts, soy, itadori tea • Ellagic acid foods: Berries, pomegranate, grapes, walnuts, blackcurrants • Ferulic acid foods: Whole grains, roasted coffee, tomatoes, asparagus, olives, berries, peas, vegetables, citrus • Astaxanthin foods: Algae, yeast, salmon, trout, krill, shrimp, and crayfish • Tea: rooibos, honeybush, dandelion • Other: Citrus, soy, rosemary, curcumin (turmeric, curry powder) **D-GLUCARIC ACID FOO SOURCES**[183] • Legumes: Mung bean seeds, adzuki bean sprouts • Fruits and vegetables: Oranges, spinach, apples, carrots, alfalfa sprouts, cabbage, Brussel sprouts, cauliflower, broccoli, grapefruit, grapes, peaches, plums, lemons, apricots, sweet cherries, corn, cucumber, lettuce, celery, green pepper, tomato, and potatoes • Genistein: Fermented soy, miso, tempeh	**INDUCERS** • Calcium D-glucarate[186] • Sulforaphane[187] • Quercetin[188] • Curcumin[188] • Fish oil • Chrysin[189]	**Micronutrient:** To assess micronutrient levels **NutriPro:** To assess genetics related to micronutrients **Gut Zoomer:** To assess for beta-glucuronidase levels

Sulfation	**INDUCERS**[183]
	• <u>Caffeine:</u> Coffee, cocoa, black tea, green tea
	• <u>Retinoic acid</u> (bioactive form of vitamin A): Meat, liver, fish, egg, dairy products, apple, apricot, artichokes, arugula, asparagus
	SULFUR FOOD SOURCES[183]
	• <u>Animal products:</u> fish, shellfish, lamb, beef, chicken, pork, duck, goose, turkey, egg, cheese
	• <u>Legumes:</u> Lentils, peas, and butter beans
	• <u>Grains:</u> Barley, oatmeal
	• <u>Vegetables and fruits:</u> Cabbage, horseradish, Brussel sprouts, leeks, cress, haricot beans. Apricots, peaches, spinach, and watercress
	• <u>Nuts and seeds:</u> Brazil nuts, almonds, peanuts, and walnuts
	• <u>Herbs and spices:</u> Mustard, ginger
		INDUCERS
		• **Molybdenum**[190]
		• **Vitamin B2**
		• **Sulfur containing compounds:**
		  ◦ N-Acetyl Cysteine
		  ◦ Taurine
		  ◦ Glutathione
		  ◦ Chondroitin sulfate/glucosamine sulfate
		  ◦ Indole-3-carbinol
		  ◦ MSM
		OTHER:
		• Magnesium sulfate (Epsom salt) baths
			Micronutrient: To assess micronutrient levels
			NutriPro: To assess genetics related to micronutrients
			Gut Zoomer: To assess for sulfate reducing bacteria

Amino Acid Conjugation	**INDUCERS** • Protein rich diet **INHIBITORS:** • Low protein diets **FOOD SOURCES OF AMINO ACIDS**[183] • <u>Glycine:</u> Animal proteins, seafood, soybean, seaweed, eggs, amaranth, peanuts, almonds, seeds (pumpkin, sunflower), lentils, bone broth, collagen • <u>Taurine:</u> Animal proteins and seafood • <u>Glutamine:</u> Animal proteins, dairy products, spinach, parsley, cabbage • <u>Arginine:</u> Animal proteins (turkey, pork, chicken, beef), seeds (sesame, pumpkin, sunflower), eggs, soybeans, butternuts, nuts (peanuts, almond, walnuts, pine nuts), legumes (lentils, mung beans, fava, white beans)	**INDUCERS**[183] • Amino acids complete supplement • Glycine • Glutamine • Taurine • Ornithine • Arginine	**Micronutrient:** To assess micronutrient levels
Methylation	**FOOD SOURCES NUTRIENTS TO SUPPORT METHYLATION**[183] • Methionine: Meat, poultry, fish, shellfish, eggs, nuts (brazil), seeds (sesame, pumpkin), spirulina, teff, soybeans • Betaine: Quinoa, beets, spinach, whole grains, seeds, legumes, prunes • Foods high in: B12, B6, folate, magnesium	**INDUCERS**[183] • B Vitamins: Vitamin B12, Vitamin B6, folate • Magnesium • Betaine • SAMe • Choline	**Micronutrient:** To assess micronutrient levels **Methylation Panel:** To assess genetics impacting methylation
Acetylation	**FOOD SOURCES OF QUERCETIN**[183] Apple, apricot, blueberries, yellow onion, kale, alfalfa sprouts, green beans, broccoli, black tea, and chili powder	**INDUCERS** • Nutrient cofactors to increase acetyl CoA production: Vitamin B1, B2, B3, B5, alpha lipoic acid • Acetyl L-carnitine: provide acetyl groups • Quercetin: 500mg/d[183]	

SUPPORT PHASE 1 DETOXIFICATION

PHASE 1 DETOXIFICATION:

This is the initial phase of detoxification, also known as functionalization. It involves adding a reactive site/group to the toxic compound (such as hydroxyl, carboxyl, or an amino group) through oxidation, reduction, or hydrolysis reactions. This allows the toxin to become hydrophilic and prepares it to move onto phase 2 of detoxification for eventual excretion from the body. The phase 1 action is generally carried out by the cytochrome P450 superfamily of enzymes (CYP450) in addition to other enzymes. These enzymes are predominantly found in the liver, but also in enterocytes, kidneys, lungs, and the brain.

ANTIOXIDANT SUPPORT:

This first step of detoxification converts the toxins to highly reactive intermediates and, in the process, forms reactive oxygen species. Therefore, it's very important to increase antioxidant status to offset oxidative damage. It's also important to understand that increased phase 1 activity may potentially contribute to more damage in the body if there is inadequate phase 2 support. For this reason, it's often recommended to upregulate phase 2 detoxification pathways prior to upregulating phase 1 detoxification pathways. Many genetic SNPs exist within the CYP450 family, that may affect somebody's ability to detox. There are also many other factors that may induce or inhibit CYP450 enzymes, such as dietary compounds and supplements to name a few.

DOWNREGULATE:

Downregulating CYP450 enzymes may be important if there is not adequate phase 2 support. Decreasing phase 1 detoxification, while supporting phase 2 detoxification can allow the body to slow the formation of the highly reactive intermediates formed from phase 1 and encourage excretion of toxins from the body.

UPREGULATE:

Upregulating phase 1 detoxification is important to facilitate detoxification and is generally recommended once there is enough support for phase 2 detoxification. Upregulating phase 1 detoxification without phase 2 support can lead to increased formation of highly reactive intermediates, which can have negative effects on the body.

PHASE 1 DETOX CONSIDERATIONS

	INHIBITORS	INDUCERS
GENERAL CYP450	• Drugs: Multiple drugs can inhibit cytochrome P450 enzymes • Foods: Grapefruit • Chronic kidney disease can decrease cytochrome P450 enzyme activity[191] • Other: Inflammation may downregulate mRNA synthesis of metabolizing enzymes[192] • Dysbiosis • Exhaustive and excessive exercise[192]	• Drugs: Multiple drugs can induce phase 1 detoxification • Foods: Cruciferous vegetables, high protein diet, char-broiled foods, alcohol • Environmental toxins • Other: Nicotine and tobacco smoke[193]
CYP1A[194]	• CYP1A1: Black raspberry, blueberry, ellagic acid, black soybean, black tea, turmeric, Lycopene[195] • CYP1A2: Apiaceous vegetables, quercetin, daidzein, grapefruit, kale, garlic, chamomile, peppermint, dandelion, turmeric, Propolis[196]	• CYP1A1: Cruciferous vegetables, resveratrol, green tea, black tea, curcumin, soybean, garlic, fish oil, rosemary, astaxanthin • CYP1A2: Cruciferous vegetables, green tea, black tea, chicory root, astaxanthin • High protein diet, fasting[197], Gingko biloba[201] • CYP1B1: Curcumin, cruciferous vegetables
CYP2A[194]	• *Not identified*	• CYP1A: Chicory root (animal study) • CYP2A6: Quercetin, broccoli
CYP2B[194]	• CYP2B: Ellagic acid, green tea, cruciferous vegetables • CYP2B1: Turmeric	• CYP2B1: Rosemary, garlic • CYP2B2: Rosemary
CYP2C[194]	• CYP2C: Green tea, black tea, ellagic acid • CYP2C6: Ellagic acid • CYP2C9: Resveratrol, myricetin (onions, berries, grapes, red wine) • Fasting[197] • CYP2C19: Kale, Ginger[198], Propolis[196]	• CYP2C9: Overnutrition[197]
CYP2D[194]	• CYP2D6: Resveratrol, garden cress, kale	• CYP2D6: Fasting[197], Valerian and Gingko biloba[201]
CYP2E[194]	• CYP2E1: Watercress[199], garlic, N-acetyl cysteine, ellagic acid, green tea, black tea, dandelion, chrysin, medium chain triglycerides, Propolis[196]	• CYP2E1: Fish oil, chicory root
CYP3A[194]	• CYP3A: Green tea, black tea, quercetin • CYP3A2: Cruciferous vegetables • CYP3A4: Grapefruit, resveratrol, garden cress, soybean, kale, myricetin (onions, berries, grapes, red wine), piperine[200]	• CYP3A: Rooibos tea • CYP3A1: Garlic, fish oil • CYP3A2: Garlic, cruciferous vegetables • CYP3A4: Curcumin, Vitamin D[192], Fasting[197], St. John's Wort and Common Valerian[201]
CYP4A[194]	• *Not identified*	• CYP4A1: Green tea • CYP4B1: Caffeic acid (coffee)
Support Phase 1	• B Vitamins: Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B6, Vitamin B12, folate • Minerals: Iron, zinc, selenium, magnesium • Other: Vitamin C, Vitamin A[192], flavonoids, indoles	
Offset Toxic Metabolites	• Antioxidants • Flavonoids • Coenzyme Q10	
Testing Considerations	• Micronutrient test: tests for nutrient deficiencies • NutriPro: To assess for genetic snps that may impact nutrient deficiencies/insufficiencies	

ASSSES & MINIMIZE RISK FROM EXPOSURE

ASSSES & MINIMIZE RISK FROM EXPOSURE

Exposure to environmental toxins as well as the process of detoxification can increase oxidative stress in the body. Consuming a diet high in antioxidants may help mitigate the risk from exposure and from the reactive oxygen species formed during phase 1 detoxification.

Pair with Organic Acids Test to assess for oxidative stress

Assess for mitochondrial dysfunction

Environmental toxins can negatively impact mitochondria for many different reasons. An organic acids test can identify whether mitochondrial markers are out of range to examine the extent of toxicity-induced mitochondrial dysfunction.

Pair with Organic Acids Test to assess for mitochondrial dysfunction

Assess gut function

Environmental toxins can change the ecosystem of the microbiome. Certain environmental toxins have been shown to correlate with intestinal permeability. Certain environmental toxins have been shown to increase dysbiotic microbes in the gut.

Pair with Gut Zoomer Test to assess the health of the microbiome

Assess for micronutrient deficiencies

Exposure to environmental toxins can contribute to micronutrient deficiencies/insufficiencies in situations when the body is using nutrient stores to facilitate detoxification processes and offset reactive oxygen species formed.

Pair with Micronutrient Test to assess micronutrient levels and NutriPro to assess genetic risk for micronutrient deficiencies/insufficiencies

GENERAL DETOXIFIATION CONSIDERATIONS

WATER

- High quality water filter for drinking water
- Visit your city's website to retrieve a report on local water quality
- Consider a whole house water filter or specific filters for shower/baths

INDOOR AIR

- Consider using an air purifier; HEPA filters are best to filter particulate particles while activated carbons and zeolite based products best filter VOC's
- If using air conditioner, change filters regularly and opt for a high MERV rating for greater indoor air filtration
- Limit products used indoors that may increase indoor air pollution, such as paints, glues, certain body care products, perfumes
- Limit new furniture that may off-gas chemicals for many years
- Include indoor plants that have air detoxifying properties, such as snake plant, english ivy, peace lily, bamboo palm, areka palm, and other air filtering plants
- Limit products that claim to "freshen" the air, such as indoor air fragrances, odor control products, candles

OUTDOOR AIR

- Limit exercise in highly polluted areas
- Avoid standing directly next to the gas tank when pumping gas, or stand upwind

FOOD

- Choose organic foods as able
- Limit consumption of packaged foods
- Consume foods high in antioxidants to offset the reactive oxygen species formed from normal phase [1] detoxification processes
- Consume foods that may help support phase 2 detoxification: cruciferous vegetables, sulfur rich foods, etc.
- Use non-toxic cookware. Consider cast iron, stainless steels or ceramic coated cookware.

BODYCARE

- Visit www.skincaredeep.org to assess ingredients and potential risks of different body care products
- Limit/avoid body care products that contain phthalates, parabens, and other potentially toxic ingredients

HOUSEHOLD

- Remove shoes when inside the home to prevent environmental toxins found outdoors from contaminating indoor environment
- Avoid/limit use of pesticides for home use (pest control, domestic animal pest control)
- Avoid/limit cleaning products with potentially harmful ingredients, opt for naturally based products
- Avoid/limit plastic Tupperware/cups and opt for glass instead

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