

Interpretive Guide



The Scope of the Toxicant Problem

Toxicity is a growing concern for both doctors and their patients. In the United States alone, there are over 80,000 chemicals registered for use.

Approximately 2,300 new chemicals are annually submitted for review to the U.S. Environmental Protection Agency (EPA); less than half of the high-volume chemicals have been tested for toxic risk to humans and only 7 percent have been assessed for developmental effects in children.¹ Unknown to many, the effects of multiple chemical exposures, or synergistic effects are rarely evaluated—researchers are only now beginning to learn of the serious and far-reaching consequences. Additionally, it can be difficult to identify which toxin the patient may have been exposed to.

These concerning facts are behind the development of the comprehensive **Toxic Effects CORE** (Chemical Occurrence & Related Exposure) Profile, which tests for exposure to multiple compounds in six categories of common environmental toxicants.



Toxic Effects

CORESM

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Turn the Tide on Toxic Exposures

Chemical Exposure

Pervasive chemical compounds have been found to disrupt the immune, nervous, and endocrine systems. As more toxicants are used in products that increase the “convenience factor” of our busy lives, there continues to be increases in infertility, certain cancers, developmental delays, asthma, chemical sensitivities, and hormonal imbalances. Environmental toxicants have been implicated in causing and exacerbating many of these conditions.

Populations at increased risk from the effects of these toxicants include:

- Infants
 - › Including in utero development and children
- Couples involved in preconception planning or infertility
- People with multiple and repeated toxicant exposures
 - › Jobs and hobbies
- People with immune impairment
- People with poor nutrient status
- People experiencing significant weight loss
 - › Post bariatric surgery
- Elderly
 - › Since toxicants bioaccumulate over time

Additionally, the impact of various exposures (whether individual, simultaneous, sequential, or cumulative over a lifetime) may not be simply additive. Instead, combinations of exposures may have synergistic effects that intensify or otherwise alter their impact, when compared with the effects of each contaminant alone.^{2,3}

The presence of toxicants can be a burden, hindering patients from responding to treatment. Practitioners searching for a patient’s underlying causes of illness should consider testing for toxicants as a priority in their assessment. The CORE Profile can help identify a patient’s specific toxic burden and allow the clinician to determine the optimal way to biotransform the toxicants and help the patient avoid further exposure.

How To Use The Toxic Effects CORE Test Results

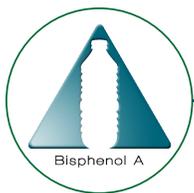
The summary of elevated toxicants indicates those compounds found at or above the 95th percentile which are indicative of exposure to higher levels of toxicants than found in the general population. Appropriate treatment may be determined by the levels of detected toxicants and/or the clinical symptoms consistent with those outlined in this interpretive guide.

To help identify possible sources of exposure, each toxicant class is summarized in the following tables, along with commonly associated health effects. This guide concludes with General Action Steps required to help relieve body burden for all toxic exposure and Specific Action Steps for indicated toxicants.



1. Overview of Tests Included in the Toxic Effects CORE Profile

Category	Alkylphenols	Organochlorines	Organophosphates	Plasticizers/Preservatives	Polychlorinated Biphenyls (PCBs) Special Organochlorine Group	Volatile Organic Compounds (VOCs)
Individual Test Profile Name	Bisphenol A	Chlorinated Pesticides	Organophosphates	Phthalates & Parabens	Polychlorinated Biphenyls (PCBs)	Volatile Solvents
All Compounds Tested For in the Complete Toxic Effects CORE Profile	BPA	DDE	DMTP	Phthalates	Dioxin-Like	Benzene
	Triclosan	DDT	DMDTP	MEtP	PCB 77	Ethylbenzene
	4-Nonylphenol	Dieldrin	DETP	MEHP	PCB 118	Xylene
		Heptachlor Epoxide	DEDTP	MEHHP	PCB 126	Styrene
		Hexachlorobenzene	Atrazine	MEOHP	PCB 156	Toluene
		Mirex	Atrazine mercapturate		PCB 169	N-Hexane
		Oxychlorodane		Parabens		2-methyl-pentane
		Trans-Nonachlor		Butylparaben	Non-Dioxin-Like	3-methyl-pentane
		Endosulfan Sulfate		Ethylparaben	PCB 74	
				Methylparaben	PCB 138	
			Propylparaben	PCB 153		
				PCB 180		



Used since the 1940s, alkylphenols today are found in common everyday products, including hair care products, cosmetics, food packaging, plastics, household cleaners, pesticides, paints, and even spermicide. Because the toxicants are an effective surfactant in both water- and oil-based scenarios, they are commonly used in detergents.

Due to their slow biodegradation, alkylphenols tend to bioaccumulate, moving up the food chain to humans. Alkylphenols are in the dust in our homes, in our food, and in our breast milk, blood, and urine.^{4,5}

2. Alkylphenols

Compound	Sources/Exposures	Toxicant Effects
Bisphenol A	Food and beverage containers, thermal sales receipts, water bottles, plastic dinnerware, baby bottles	In population based studies, urinary BPA levels were significantly associated with heart disease, PAD and hypertension, independent of traditional risk factors.
Triclosan	Deodorants, toothpastes, shaving cream, mouth wash, cleaning supplies	
4-Nonylphenol	Stabilizing agents, PVC food packaging, emulsifying agents, wetting agents	

Shankar A, Teppala S, Sabanayagam C. 2012 Sep;120(9):1297-300.

Shankar A, Teppala S. *J Environ Public Health*. 2012;2012:481641.

Meizer D, Osborne NJ, Henley WE, et al. *Circulation*. 2012;125(12):1482-1490



Organochlorines are compounds that contain carbon, chlorine, and hydrogen; the most infamous organochlorine being DDT.

Long used as insecticides in a wide variety of applications, these compounds are ubiquitous in the environment. Because their chlorine-carbon bonds are very strong, they do not break down easily. Therefore, despite the long-term banning of most compounds within this class in the U.S., these compounds persist in the environment today.

Organochlorines are highly insoluble in water, but bioaccumulate in fats, resulting in high fat meats, dairy, and fish becoming a major source of food-borne exposure.⁶

3. Organochlorines

Compound	Sources/Exposures	Toxicant Effects
DDT, DDE (DDT breakdown product)	Used agriculturally until 1972, currently found in meat, poultry, dairy products, and fish	Several Chlorinated Pesticides have been noted as persistent organic pollutants (POP) by the United Nations Environment Programme Governing Council. In humans, reproductive, developmental, behavioral, neurologic, endocrine, and immunologic adverse health effects have been linked to POPs.
Dieldrin	Used as an insecticide on corn and cotton from 1950s until 1978	
Heptachlor Epoxide	Used as a residential termiticide until 1988	
Hexachlorobenzene	Used as a pesticide until 1965, as fungicide in cereal grains, and as a wood preservative by-product	
Mirex	Used as a pesticide for fire ant control until 1978, and as a flame retardant additive	
Oxychlordane	Metabolite of chlordane and nonachlor compounds used agriculturally until 1974 and residentially until 1988	
Trans-Nonachlor	Chlordane metabolite used agriculturally until 1974, as termiticide until 1988	NHANES correlation studies have confirmed an association between type 2 diabetes and chlorinated pesticides in a general urban population, as well a risk factor in peripheral arterial disease (PAD).

Airaksinen R., *Diabetes Care*. 2011 Sep;34(9):1972-9.

Min, J.Y., *Atherosclerosis*. 2011 Sep;218(1):200-6.

The International Programme on Chemical Safety (IPCS) POPs. 1995; www.chem.unep.ch/pops/ritter/en/ritteren.pdf

Endosulfan Sulfate	Currently used agriculturally (cotton, tea, fruits, vegetables, tobacco, grains), and as a wood preservative
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No national percentiles have been set for Endosulfan Sulfate. Detected levels are above the Metamitix limit of quantification (0.34 ppb).



“Organophosphates” is a generic term to include all insecticides that are derived from phosphoric acid and contain phosphorus. They are considered by some experts to be the most toxic of all pesticides to vertebrate animals.

Organophosphates inhibit the cholinesterase enzymes of the nervous system, resulting in the buildup of acetylcholine, which interferes with neurological and muscular functions.⁷

4. Organophosphates

Compound	Sources/Exposures	Toxicant Effects
Dimethylthiophosphate (DMTP) Dimethyldithiophosphate (DMDTP) Diethylthiophosphate (DETP) Diethyldithiophosphate (DEDTP) Atrazine Atrazine mercapturate	Crops, trees, ornamentals, lawn treatments, Insect control (mosquito, fleas, termites), livestock	Epidemiologic studies suggest that prenatal exposure to organophosphates is associated with poorer neurobehavioral development, and postnatal exposure has been correlated with behavioral problems, and impairments in short term memory, executive function, and motor skills. Effects of acute high dose or high-dose worker exposures include neurological dysfunction.

Center for Disease Control and Prevention, The Fourth National Report on Human Exposure to Environmental Chemicals, 2009.
www.cdc.gov/exposurereport
 Boucharde MF, et al., *Pediatrics*. May 17 2010.
 Hoppin, J.A., et al. *Ann N Y Acad Sci*, 2006.



Phthalates are compounds added to plastic to make it more flexible. Known as plasticizers, these compounds are also added as stabilizers to other product groups. Therefore, phthalates can be found in a wide array of items, as seen in the table below. Phthalates are easily released from the original product; as plastic ages, phthalate release accelerates.

Most Americans tested by the Centers for Disease Control (CDC) have metabolites of multiple phthalates in their urine.⁸ Parabens are the most widely used preservative in personal care items⁸ and appear in over 10,000 of the 25,000 products analyzed in the Environmental Working Group’s Skin Deep database.^{9,10}

Although parabens are still considered safe by the FDA at certain levels of use, a 2004 study raised questions concerning the relationship between parabens and breast cancer; parabens are estrogen mimics and may disrupt hormonal function.¹¹

5. Plasticizers/Preservatives

Compound	Sources/Exposures	Toxicant Effects
Phthalates MEHHP, MEHP, MEOHP, MEtP	Plastics, cosmetics, perfumes, medications, medical bags, commonly appears as “fragrance”	Possible steroid hormone disruption; <ul style="list-style-type: none"> • Synergistic effect may enhance estrogen receptor response • Impaired male reproductive development • Endometriosis Have been linked to obesity in research.
Parabens Butylparaben, Ethylparaben Methylparaben, Propylparaben	Shampoo and conditioner, shave gels, cosmetics, personal lubricants, deodorant, and food additives	

Reddy BS, Rozati R, Reddy BV. *Bjog*. May 2006;113(5):515-520.
 CDC. Biomonitoring Summary: Phthalates Overview. National Biomonitoring Program 2012;
www.cdc.gov/biomonitoring/DEP_BiomonitoringSummary.html
 Stahlhut RW, van Wijngaarden E, Dye TD, Cook S, Swan SH. *Environmental Health Perspectives*. Jun 2007;115(6):876-882.

Understand the Far-Reaching Effects of Environmental Toxins



Over 200 PCBs were introduced into our environment before 1977. The CDC currently measures for 15 PCBs in population studies, commonly finding 10 of them in people tested. Of those 10, six have known negative health effects published in the medical literature.¹²

A special category of organochlorines, PCBs have gained notoriety in recent years due to the emerging information on their persistence in the environment and their demonstrated potential for soil-to-human biomagnification.

7. Polychlorinated Biphenyls (PCBs)

Compound	Sources/Exposures	Toxicant Effects
Dioxin-Like PCBs PCB 118; PCB 126 PCB 156; PCB 169 PCB 77	Contaminated food (high fat dairy and meat, Atlantic farmed salmon and other farmed fish), contaminated water, old electrical fixtures,	Studies in humans provide supportive evidence for potential carcinogenic and non-carcinogenic (immune, reproductive, neurologic and endocrine) effects of PCBs. PCBs have been correlated with lowered IQs in children exposed prenatally.
Non-Dioxin-Like PCBs PCB 74; PCB 138 PCB 153; PCB 180	breast milk from mothers with elevated levels.	

Hatcher-Martin, J. M., et al., *Neurotoxicology*, 2012 Aug 18.
De Coster, S., et al., *Environ Health*, 2008 Jun 3;7:26.
Bosch de Basea, M., et al., 2011 May;68(5):332-8.
Cohn, B. A., et al., *Reproductive Toxicology*, 2011 Apr;31(3):290-6.
Stewart, P. W., et al., *Environmental Health Perspectives*, 2008.0ct;116(10):1416-22.



According to the Occupational Safety & Health Administration (OSHA), millions of workers are exposed to solvents on a daily basis. Volatile solvents are also heavily used in the average home.

Common household products, which often contain organic solvents, include cleaning and polishing fluids, spray-on personal care items, nail-polish removers, contact adhesives, paint, and lacquer thinners.

Indoor air fresheners and fabric deodorizers are a particularly common source of exposure, as are gasoline and cigarette smoke. These organic solvents are also sometimes purposely inhaled for psychoactive effects.¹³

6. Volatile Solvents

Compound	Sources/Exposures	Toxicant Effects
Benzene	Gasoline, cigarette smoke, indoor air fresheners, glues, paints, well water, and detergents	Exposure to Volatile Solvents in humans has resulted in ocular and respiratory irritation; neurologic symptoms (headaches, loss of coordination); nausea; as well as hepatic, renal and CNS damage. Some VOCs have been shown to be carcinogenic in animals; some are suspected or known to be carcinogenic (benzene) in humans.
Ethylbenzene	Gasoline and styrene, paints, inks, varnishes, and glues, pesticides, tobacco products, groundwater	
Styrene	Primarily used in the production of polystyrene plastics, and resins. Airborne exposures: cigarette smoke, auto exhaust, photocopies. Ingestion exposures: food heated or stored in styrofoam containers	
Toluene	Airborne exposures: paint fumes, glues, solvents, gasoline, nail polish, stain removers, carburetor cleaners, cigarette smoke, and auto exhaust. Higher levels are found in smokers, regular drinkers, and those exposed to fumes	
Xylenes -m, p-xylene -o-xylene	Used in printing, rubber, and leather industries. Airborne exposures: gasoline, auto exhaust, cigarette smoke, fumes from paint, varnish, cleaners. Dermal exposure: direct contact	
n-Hexane 2-Methylpentane 3-Methylpentane	Used in glues, adhesives, and gasoline. Exposure sources: gasoline exhaust, paints, quick-drying glues and adhesives, jet fuel and jet exhaust. (Hexane consists of n-hexane and its isomers of 2-methylpentane and 3-methylpentane)	No national reference ranges are established for hexane, 2- and 3- methylpentane and iso-octane. Percentile ranges are based on patient samples analyzed at Metamatrix.
Iso-octane	A component of gasoline, usually in a mixture of related hydrocarbons	

Center for Disease Control and Prevention, The Fourth National Report on Human Exposure to Environmental Chemicals, 2009. www.cdc.gov/exposurereport

Environmental Factors Contribute to More Than 25% of All Diseases*

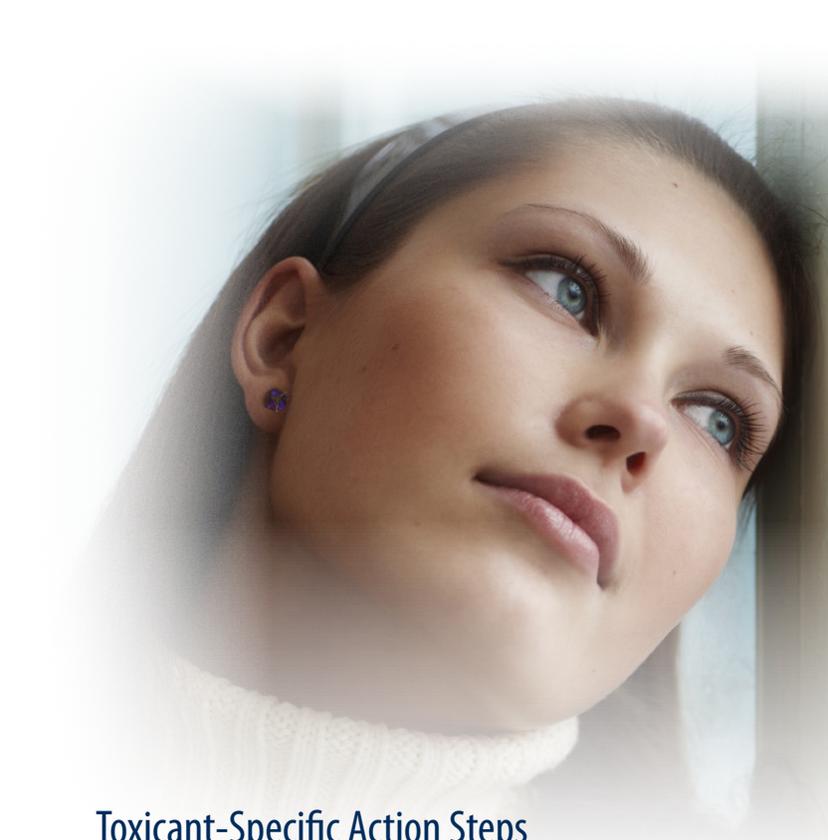


General Action Steps

Identify the most likely exposure source(s) using the previous tables (see also Additional Resources on Individual Toxicants) and take steps to avoid further exposures. This may mean discontinuing the use of certain household cleaning products or personal hygiene preparations, avoiding commonly contaminated foods, and substituting organic foods whenever possible.

- Protect against toxicant damage from:
 - › Oxidative stress
 - › Inflammation
 - › Mitochondrial injury
 - › Minimize such damage through the use of nutrients and botanicals, such as: vitamin C, vitamin E, alpha lipoic acid, B-complex, magnesium, milk thistle, curcumin.
- Support and Stimulate Liver Biotransformation (Phases 1 & 2)
 - › Support biotransformation with proper diet and supplementation (nutrients and botanicals that are substrates for and inducers of Phase 2 pathways).
 - › The majority of these compounds are cleared from the body after undergoing oxidation, followed by a variety of conjugation reactions with substrates like glucuronic acid, glycine, or glutathione. Some compounds, that are frequently used as dietary supplements to support or stimulate the biotransformation pathways in the liver and protect tissues and cells from toxic effects, are:
 - › Taurine
 - › N-Acetyl cysteine
 - › Glycine
 - › Lipoic acid
 - › Glutamine
 - › Milk thistle
 - › Exercise stimulates hepatic detoxification enzymes.¹⁴
- Enhance the clearance of environmental toxins (Phase 3)
 - › Reduce renal and hepatic recycling. Exercise promotes excretion via the kidneys and skin.¹⁴
 - › Sauna therapy has been used to reduce the presence of fat-soluble toxicants.¹⁵
 - › Ensure good intestinal function and bacterial balance to promote elimination of toxicants and toxicant by-products. Detoxification by-products that are passed into the gut may be broken down by bacterial enzymes and released for absorption back into the blood. Supplements, such as calcium D-glucarate, may be used to reduce this process, and steps to improve intestinal bacterial balance can help to restore healthy elimination of toxicants.¹⁵
 - › Support phase 3 clearance of toxicants through the use of products such as rice-bran fibers, chlorophyll, and fat-binders. Increasing these foods in the diet, or using daily supplementation, will slowly increase the excretion of these compounds from the body.
 - › In addition to the chlorophyll containing agents, polyphenols (found highest in white and green teas) have been shown to increase fecal excretion of fat-soluble toxins.¹⁶

* U.S. Department of Health and Human Services Agency for Toxic Substances and Disease Registry (ATSDR)



Toxic Effects Run Deep... Test Results Provide Actionable Results

Toxicant-Specific Action Steps

Alkylphenols

- Avoid polycarbonate containers that contain BPA, which usually have the symbol #3 or #7 on the bottom.
- Look for BPA-free cans and containers and reduce your use of canned foods overall.
- When possible, opt for glass, porcelain, or stainless steel containers, particularly for hot food or liquids.
- Avoid handling store receipts, which have been found to be a source of BPA.
- Use baby bottles that are BPA-free.
- Do not microwave polycarbonate plastic food containers, as it will increase release of BPA exposure.
- To minimize 4-nonylphenol exposure, do not heat food in plastic cling-type materials.

Chlorinated Pesticides (CPs)

- Avoid foods found to contain the high levels of Chlorinated Pesticide
 - › Non-organic butter – high in DDE, HCB
 - › Farmed Atlantic salmon and certain lake-caught fish – high in DDE, dieldrin, HCB, mirex
 - › Non-organic greens (spinach, collards) – high in DDE
 - › Non-organic cheeses (cream cheese, cheddar, American) – high in DDE, dieldrin, HCB
 - › Non-organic fatty meats (lamb, ground beef) – high in DDE, HCB

- Enhance clearance of persistent toxins with cleansing protocols.¹⁵
- Chlorophyll and chlorophyll-containing foods may be effective at increasing the excretion of fat-soluble persistent toxins through the feces.^{17, 18}

Organophosphates (OPs)

- Supplementing with nutrients that stimulate detoxification (esp. taurine, glycine, and n-acetylcysteine) may be useful in reducing body burden of OPs.
- Supplementing with antioxidants vitamin E, vitamin C and alpha lipoic acid may protect against OP-induced oxidative stress.^{19, 20}
- Evaluation of oxidative stress can be useful for monitoring exposed people.¹⁹

Plasticizers and Preservatives

- Look for labels indicating “Phthalate- or Paraben- Free.”
- Oligoantigenic diets containing whole, organic foods, including dark colored vegetables, nuts, seeds, and whole grains along with the detoxification stimulating components from such foods are usually recommended for patients with elevated levels of urinary phthalates.²¹
- Increasing phthalate-free fluid intake may improve rates of phthalate excretion, leading to lowering of tissue levels.



Polychlorinated Biphenyls (PCBs)

- Avoid known contaminated foods, especially farmed Atlantic salmon and fish from the Great Lakes, non-organic butter, and non-organic meats.
- Daily use of rice bran fiber has been documented in several studies in Japan to increase the clearance of PCBs.²²⁻²⁴
- Chlorophyll and chlorophyll-containing foods may be effective at increasing the excretion of fat-soluble persistent toxins through the feces.^{17, 18}

Volatile Organic Compounds

- Keep area well ventilated when working with any type of volatile solvent.
- Avoid the use of indoor air fresheners.
- Avoid breathing household cleaning products and begin transitioning to non-toxic cleaners.
- Avoid heating or eating foods in Styrofoam containers (especially hot drinks).
- Volatile solvent detoxification products that have been passed into the gut may be broken down by bacterial enzymes and released for absorption back into the blood. D-Glucaric acid (as calcium D-glucarate, for example) may be used to reduce this process.
- Supplementation of vitamin C, selenium, glycine, glutamine, taurine, N-acetylcysteine, and alpha lipoic acid has been proposed.²²

Retesting

If initial levels are found extremely high, then retesting for individual toxicant(s) categories may be done in monthly intervals to ensure that effective steps are being taken in an effort to decrease the high risk of adverse health effects. For moderate or mild elevations, intervals of four to six-plus months or more are commonly employed to give assurance of improvements and to detect any new exposures that may occur.

Complementary Test Panels

Assess detoxification ability with the organic acid analysis, amino acid analysis, and genetic-predisposition testing. These tests can aid in designing appropriate detoxification protocols for patients.

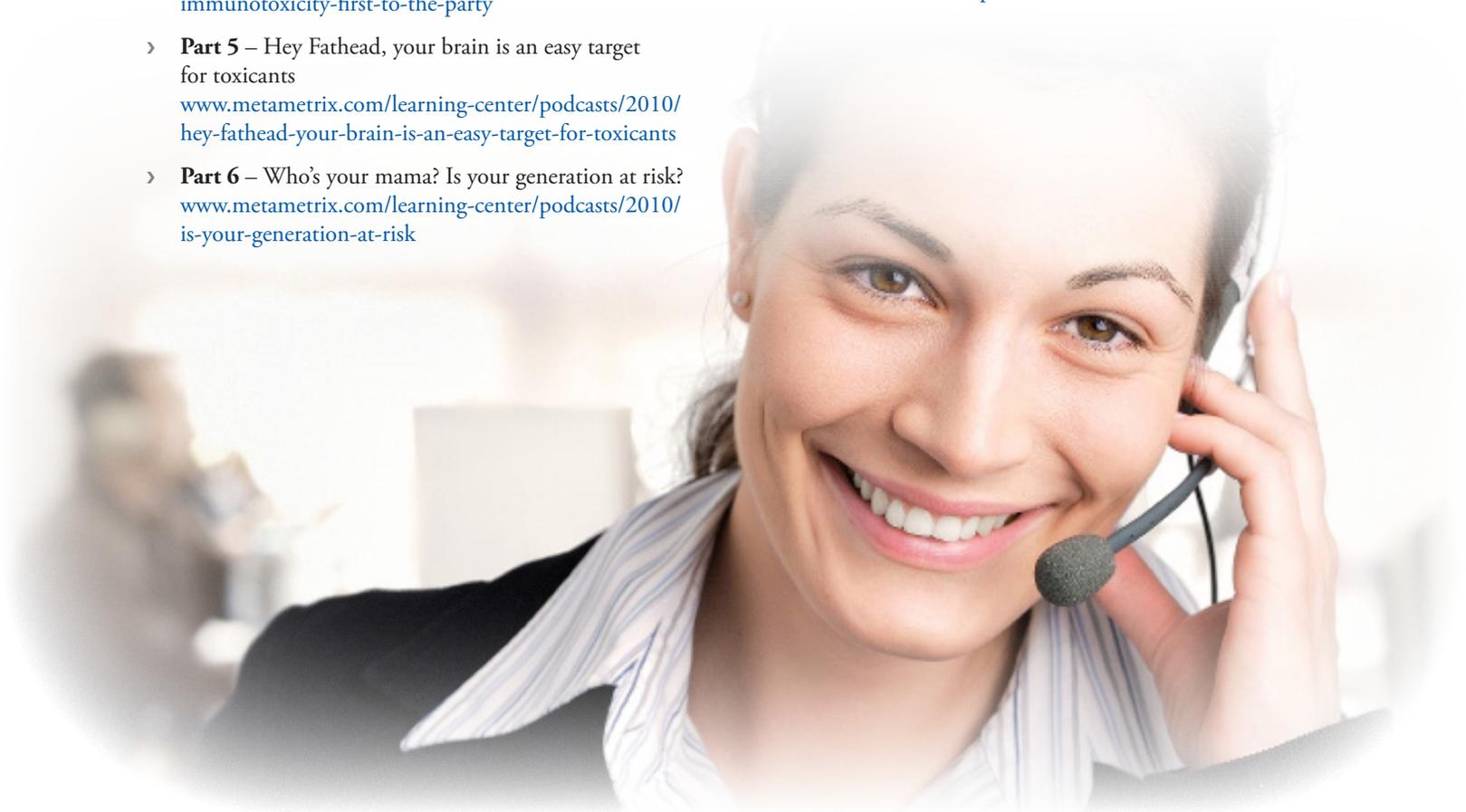
Additional Resources

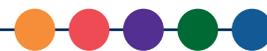
- Metamatrix Learning Center
 - › www.metamatrix.com/learning-center
- Walter J. Crinnion, ND – Six part audio series on environmental toxicants
 - › **Part 1** – Why is it important to understand total toxic body burden?
www.metamatrix.com/learning-center/podcasts/2010/why-it-is-important-to-understand-total-toxic-body-burden
 - › **Part 2** – Why should we test for toxic exposure?
www.metamatrix.com/learning-center/podcasts/2010/why-should-we-test-for-toxic-exposure
 - › **Part 3** – How do toxicants affect mitochondria?
www.metamatrix.com/learning-center/podcasts/2010/how-do-toxicants-affect-mitochondria
 - › **Part 4** – Immunotoxicity—First to the party
www.metamatrix.com/learning-center/podcasts/2010/immunotoxicity-first-to-the-party
 - › **Part 5** – Hey Fathead, your brain is an easy target for toxicants
www.metamatrix.com/learning-center/podcasts/2010/hey-fathead-your-brain-is-an-easy-target-for-toxicants
 - › **Part 6** – Who’s your mama? Is your generation at risk?
www.metamatrix.com/learning-center/podcasts/2010/is-your-generation-at-risk

Additional Resources on Individual Toxicants:

After identifying the specific categories of concern through the CORE profile, more extensive information for each toxicant category and individual compounds may be found by visiting:

- www.metamatrix.com/files/test-menu/interpretive-guides/BPA-IG.pdf
- www.metamatrix.com/files/test-menu/interpretive-guides/Chlorinated-Pesticides-IG.pdf
- www.metamatrix.com/files/test-menu/interpretive-guides/OP-IG.pdf
- www.metamatrix.com/files/test-menu/interpretive-guides/Phthalates-Parabens-IG.pdf
- www.metamatrix.com/files/test-menu/interpretive-guides/PCBs-IG.pdf
- www.metamatrix.com/files/test-menu/interpretive-guides/Volatile-Solvents-IG.pdf





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63 Zillicoa Street
Asheville, NC 28801

800.522.4762
www.gdx.net

Atlanta

3425 Corporate Way
Duluth, GA 30096

800.221.4640
www.metamatrix.com

London

Parkgate House
356 West Barnes Lane
New Malden Surrey, KT3 6NB

020.8336.7750
www.gdxuk.net

Toxic Effects CORE Can Benefit Patients with These Issues



PEOPLE WITH HIGH RISK JOBS/HOBBYS



PRECONCEPTION – INFERTILE COUPLES



NEUROLOGICAL DISORDERS



IMMUNE SYSTEM DISORDERS



Toxic Effects CORE Profile

* Test #1765 Toxic Effects CORE includes:

- Bisphenol A
- Chlorinated Pesticides
- Organophosphates
- Phthalates and Parabens
- Polychlorinated Biphenyls (PCBs)
- Volatile Solvents

Specimen Requirements

- Urine, 12 ml (refrigerated)
- Serum, 8 ml (refrigerated)
- Whole Blood, 14 ml (refrigerated)

Tests Available for Follow-up

- * Test #0740 Phthalates and Parabens
- * Test #0760 Chlorinated Pesticides
- * Test #0761 Polychlorinated Biphenyls
- * Test #0762 Volatile Solvents
- * Test #0763 Organophosphates
- * Test #0764 Bisphenol A (BPA)

CPT codes, turnaround times, sample reports, and additional information is available online at www.metamatrix.com/tecore

* Not available in NY

Toxic Effects
CORE