

Xenobiotics & Persistent Organic Pollutants – Preludes to a Silent Spring

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In 1962 Rachel Carson, a marine biologist turned conservationist, published *Silent Spring*, a book that brought to the public's attention the effects of man made chemicals on the environment. Chemical companies, who assured us that substances such as DDT and other pesticides were not harmful to humans, met the book with severe criticism. Carson's book set the stage for the development of the environmentalist movement worldwide. In the intervening 52 years since its release, we have continued to develop and pour into the environment additional chemicals that are now termed Xenobiotics and Persistent Organic Pollutants.

A xenobiotic is defined as an artificial man made chemical that is found in an organism that is not normally produced or expected to be present. As an example, drugs such as antibiotics are xenobiotics because the body does not produce them, nor are they part of a normal diet. Natural compounds can also become xenobiotics if they are taken up by organisms that normally do not make or ingest them. An example here is hormones such as estrogens in poultry or fish. Most often the term is used to describe pollutants such as dioxins and polychlorinated biphenals and their effects on the environment.

Persistent Organic Pollutants or POP's are a broad category of synthetic chemicals including polychlorinated biphenyls (PCBs), dioxin, chlordane, and DDT. POP's are pervasive chemicals, more of which are being developed on an ongoing basis. Both terms are often used interchangeably.

POP's can be categorized as follows:

1. Hormone disruptor biocides (pesticides, fungicides, mitocides)
 - Cholinesterase inhibitor organophosphate pesticides
 - Halogenated pesticides.
 2. Solvent residues
 - Chlorinated compounds (chloroform, methylene chloride, ethylene chloride)
 - Other halogenated compounds (brominated, fluorinated, iodinated)
- used most commonly as artificial food dye colorants, as radio-contrast agents, and art materials.

Even though some POP's have been banned or are restricted in use by some countries, POP's are, as their name suggests, persistent in the environment. They evaporate slowly into the atmosphere and aquifers and disperse around the globe. Living organisms then concentrate these fat-soluble chemicals in fatty tissues. Because they are man made substances, the ability of the micro biota that normally breaks down natural substances for recycling, is nonexistent. Therefore, POP's and xenobiotics remain as permanent substances constantly being recycled through the food chain.

Adverse effects on human health can begin at thresholds below direct detection. In the case of dioxin, PCB, polybrominated biphenyl (PBB), and related compounds, human health risks emerge at the parts per trillion (ppt) level. This is in contrast to most laboratory tests that are only able to measure down to parts per million (ppm) levels of detection. In other words, we now routinely have biological health effects at amounts of materials in our bodies below our ability to detect them.

Many of these compounds have been found in breast milk and cord blood meaning that infants are not only exposed in-utero, but after they are born with breast feeding. It has only been within the past few years that research has intensified to determine what effects these chemicals have on humans.

These compounds are now being found to exert a variety of effects on the human body such as disrupting enzyme systems, mimicking estrogen, central nervous system depression, anemia, bone marrow depression, cause allergic reactions and many are carcinogenic.

The bad news is that they are pervasive and exposures are difficult to avoid. The good news is that they are relatively easy to avoid if sources are known, as well as eliminate.

Screening tests for **Xenobiotic** and **Persistent Organic Pollutants** requires a first morning urine which will contain a larger concentration of the metabolite. If present, a detoxification program will help to eliminate the metabolites while an on-going antioxidant regimen will help to keep them from building up from future exposures. For more information, please do not hesitate to contact your physician.

Benzene & Its Metabolites

The **Benzene metabolite, Trans, trans-muconic acid** is a component of crude and refined petroleum products and therefore found with automotive emissions, poor emission-control devices on older vehicles, poor maintenance practices, automotive-refueling operations and industrial emissions. It is also a component of discharges of industrial wastewater from chemical plants, chemical manufacturing sites, and petrochemical and petroleum industries.

It is a by-product of various combustion processes such as wood burning, organic wastes, and tobacco smoke. First and second-hand smoke accounts for the largest source of benzene exposure for the general public. The amount of benzene in a single cigarette may vary from 5.9-90 micrograms depending upon the brand.

It is also used in the manufacture of Styrofoam, resins, synthetic fibers and rubbers, gums, lubricants, dyes, glues, paints, and marking pens and is used as a solvent in scientific labs, industrial paints, adhesives, paint removers/strippers, degreasing agents, carburetor cleaner, rubber cements, some arts and crafts supplies, manufacture of faux leather and rubber goods.

Sorbic acid and potassium sorbate, common food preservatives, are metabolized to muconic acid, which may therefore cause elevations of this marker. Sources include;

processed cheese slices and spreads, salad dressings, mayonnaise, flavored drinks, canned foods, and baked goods.

Exposure to **Trans, trans-muconic acid** can cause a lowering of blood parameters such as hematocrit and haemoglobin levels, erythrocyte, leukocyte, and platelet counts; bone marrow depression which may lead to aplastic anemia, leukaemia, or thrombocytopenia. It is a known human carcinogen, is genotoxic and causes skin and eye irritation as well as central nervous system depression.

Benzene and its metabolites accumulate in lipid depots. Therefore, with weight loss stores are released which may cause symptoms. Following inhalation, most benzene is excreted through exhalation unchanged. Benzene is metabolized by the cytochrome P-450 system in the liver, is dependent oxidase enzymes and excreted as conjugated derivatives (sulfates and glucuronides) in the urine. This is all the more reason to maintain good liver function.

Paraben Metabolite Para-Hydroxybenzoate

Parabens are esters of para-hydroxybenzoic acid, are widely utilized and sources of exposure are derived from its use as an antimicrobial and as a preservative and for flavoring food. It also is found in cosmetic and pharmaceutical formulations to increase shelf life and may also be derived from bacterial metabolism in the gut. Some parabens are found naturally in plant sources such as methylparaben that is found in blueberries where it acts as an antimicrobial agent.

Body care products such as sprays, fragrances, conditioners, shampoos, hair gels, deodorants, soaps, hand sanitizers, facial masks and foundations, sunscreens, self-tanners, hair removal creams and shaving gels, nail and skin creams, baby lotion all have parabens.

Pharmaceuticals such as injectable drugs, antacids, suppositories, Benadryl™ cream, hydrocortisone creams and ointments, medicated pain-relieving patches, mentholated vapor rubs, chapstick, antifungal and antibacterial preparations contain parabens.

Food products such as packaged meats, fish and poultry, mayonnaise, oils, salad dressings, catsup, pickles, relishes, processed fruits and vegetables, frozen dairy products, cakes, pies, pastries, icings, jellies and jams, beers and ciders, soft drinks, fruit juices, syrups, and some candies.

Exposure to parabens can result in allergic contact dermatitis. Parabens have been found to exhibit estrogenic activity and decreased testosterone levels and sperm counts have been demonstrated in animal studies. Parabens are becoming increasingly controversial however, because they have been found in breast cancer tumors. To date no direct link between parabens and cancer have been established. Another concern is that the estrogen-mimicking aspect of parabens may be a factor in the increasing prevalence of early puberty in girls.

Parabens are metabolized by hydrolyzing the alkyl esters of para-hydroxybenzoic acid, to para-hydroxybenzoate, the main metabolite of parabens. This occurs via tissue esterases found in skin, subcutaneous fat, liver and kidney. Bioaccumulation of parabens may result from chronic exposure. Antioxidants will lower exposures and help to eliminate them from the body.

Phthalic Acid Ester Metabolite Phthalate

Phthalic acid esters are used in the manufacture of plastics in order to soften the resins and impart flexibility. They are one of the most widely used plasticizers for the manufacture of polyvinyl chloride (PVC) plastics utilized in vinyl flooring and tile, wall coverings, pool liners, tool handles, insulation of wires and cables, garden hoses, construction materials, weather-stripping, canvas tarps, upholstery, some food wrappers and containers. They are also found in medical equipment containing flexible plastics such as blood bags and tubing, haemodialysis equipment, children's toys, dishwasher baskets, notebook covers, flea collars, faux leather, shoe soles, traffic cones, latex adhesives, dyes, some pharmaceutical and pesticide formulations.

Detergents, lubricating oils, automobile parts, automobile undercoating, carpet backing, solvents, and personal-care products such as soaps, shampoo, hair spray, nail polish, and toothbrushes, baby-care products also contain phthalic acid esters.

Toxicity of phthalate esters, acting as metabolic disrupters, through accumulation of quinolinic acid. This may be of concern with a tryptophan rich diet and concomitant exposure to phthalate esters as they disrupt tryptophan conversion. They also act as an endocrine disrupting chemical (EDC) with young infants being especially vulnerable to their effects as they have been implicated in alterations found in development of the male reproductive system in utero and infancy. Developmental and morphological abnormalities including deficits in behavior and cognition have also been reported. More recently there have been reports of decreased sperm production in adult males exposed to environmental levels as well as their association with increased waist circumference and insulin resistance in adults.

Phthalates are hydrolyzed in the gut by pancreatic lipase yielding ester derivatives, which are rapidly absorbed. These phthalate esters are metabolized in the liver by the cytochrome P-450 dependent multifunction oxidase enzymes into glucuronide conjugates and excreted in the urine. Phthalates and their metabolites accumulate in lipid depots and may bioaccumulate due to chronic exposure.

Because of their pervasive use, exposure to phthalic acid esters and their metabolites is almost impossible to avoid. Therefore detection and a good nutritional or supplemental antioxidant program is a must in order to remove and prevent build up.

Styrene and its Metabolites: Mandelate, Phenylglyoxylate

Styrene is used in the manufacture of synthetic rubbers, synthetic latex, polyesters, and plastic products and is supplied primarily from the petroleum industry. Raw materials for the manufacturing of styrene are benzene and ethylene. Metabolites of styrene are **mandelate** and **phenylglyoxylate** and are found in auto emissions, tobacco smoke and from building materials, especially carpet backing. Low-level exposure may occur through ingestion of food products packaged in polystyrene containers and they are found in toys, craft materials, house wares, electrical and thermal insulation, fiberglass and Styrofoam cups.

Long-term exposure can lead to central nervous system depression, lightheadedness and dizziness, nausea and feeling drowsy. There may be an impairment of one's balance and a slowing of reaction time. Difficulty concentrating has been reported and styrene

and its metabolites have been shown to cause mucous membrane irritation and dermatitis. They are also known to be genotoxic.

As with other xenobiotics, Styrene is metabolized in the liver by the cytochrome P-450 dependent multifunction oxidase enzymes, into its epoxide derivatives. Styrene oxides are also conjugated with glutathione. Styrene and its metabolites accumulate in lipid depots and its slow elimination suggests the possibility for bioaccumulation from chronic exposure. As with other xenobiotics, accumulation occurs quickly but they are relatively easy to eliminate by avoidance and making sure that you are consuming a high fiber diet and lots of antioxidants.

Toluene Metabolite Hippurate

Toluene and its metabolite **Hippurate** are produced from petroleum refining. They are blended into gasoline as a component to increase the octane number and thus the horsepower of the engine. Therefore they are abundant byproducts of automotive and aircraft emissions, poor emission-control devices on older vehicles, poor maintenance practices, high-density traffic locales, gasoline filling stations, refineries and tobacco smoke. The amount of toluene in a single cigarette may vary from 80 to 100 micrograms.

Toluene is also used as a solvent carrier in paints, inks, thinners, coatings, adhesives, degreasers and even pharmaceutical products. Household aerosols such as spray paint cans, glues, varnishes, shellac, rust preventatives and solvent-based sanitizing agents and germicides. Additionally they are found as additives in cosmetic products and are taken into the body mainly by inhalation of vapors.

Toluenes and Hippurate exert a depressive or excitatory effect on the central nervous system which can manifest as euphoria followed by disorientation, tremulousness, and mood swings. Also found are tinnitus, double vision, hallucinations, difficulty with speech, ataxia, convulsions, and even coma. Initial symptoms may be irritation of the eyes, nose and throat, dizziness, and problems with taste and smell. Drowsiness, headache, impaired cognitive and motor function, insomnia, and anorexia can all occur. Solvent abuse through “sniffing” toluene containing products may lead to gross disorientation, neurological impairment and death.

Toluene is metabolized in the liver by cytochrome P-450 dependent multifunction oxidase enzymes conjugated principally with glycine, and excreted in the urine as hippuric acid. Smaller amounts may be conjugated with glucuronic acid. Minor amounts undergo hydroxylation to cresols, which are excreted in the urine as sulfate, or glucuronide conjugates.

Under conditions of chronic exposure, significant uptake of toluene into fat tissue may occur where it stays until mobilized with weight loss. Effects are reversible on cessation of exposure, but are increasingly severe and persistent with increasing concentration and/or duration of exposure.

Toluene interferes with the biotransformation of other compounds in the liver, thus making them more toxic.

Trimethylbenzene Metabolite 3,4-Dimethylhippurate

Production of **Trimethylbenzene (TMB)** and its metabolite **3,4-**

Dimethylhippurate (3,4-DMH) occurs during petroleum refining. Its primary use is as a motor fuel additive, so it is found in emissions from gasoline engines in autos, lawn mowers or anything that uses petroleum as a power source. Poor emission-control devices on older vehicles, poor maintenance practices and diesel engine exhaust are a significant source.

TMB and 3,4- DMH are also used as solvents in coatings, paint thinners, wood preservatives, cleaners, dry cleaners, degreasers, aerosols, pesticides, printing and inks. They are also used in the manufacture of pharmaceuticals, asphalt products, lacquers, varnishes, dyes, and perfumes.

These chemicals produce a number of effects upon the body when exposed to high or persistent levels. They can cause irritation of mucous membranes resulting in a watery and mucus discharge, skin rashes, dizziness, a sensation of “drunkenness”, fatigue, headache, anxiety and nervousness.

Cyanosis (poor circulation to the skin), cognitive and motor impairment, shortness of breath, episodes of increased perspiration and cardiac arrest can also occur. Diarrhea, abdominal pains, nausea and vomiting as well as blurred vision have been reported.

Because of their lipid solubility, they are highly neurotoxic resulting in a constellation of low frustration tolerance, lack of initiative, apathy, depression, and irritability termed “painter ’s syndrome”. They can also decrease erythrocyte, leukocyte and platelet counts, are carcinogenic and can cause glomerulonephritis and renal dysfunction. They are lipophilic and accumulate in fat and fatty tissues where they remain until mobilized during weight loss.

TMB and 3,4- DMH are metabolized in the liver by cytochrome P-450 dependent multifunction oxidase enzymes, conjugated with glucuronic acid, glycine, or sulfates and eliminated from the body by urinary excretion.