**Born and Dying in a Toxic World Part 2:**

# The Neurological Implications of Testing for Environmental Pollutants

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Last month, I addressed the risk that losing weight can release environmental toxins stored in adipose tissue, and the importance of having all patients who are on a weight loss regimen undergo a Comprehensive Urinary Metabolic Profile (organic acids test) with an Environmental Pollutants Profile. I mainly discussed the role of these released toxins in carcinogenesis. This month, I am going to review the studies in the medical literature that demonstrate these same toxins are associated with neurological disorders such as autism and Alzheimer's disease. This is yet another reason why testing for environmental pollutants is critical—not just in patients undergoing weight loss but also in patients who are attempting to become pregnant, in children, and in seniors. Really, environmental pollutant testing should be a foundational part of any clinician's practice.

## Environmental Toxins Hiding Around Every Corner

Parabens, phthalates, toluene, and benzene are toxins implicated in neurological disorders. Parabens are antifungal and antibacterial chemicals widely found in personal care products such as soap, shampoo, cosmetics, and perfume. These chemicals are absorbed through the skin. They are classified as endocrine disrupters and estrogen mimics and damage the mitochondria.[1,2] Phthalates are endocrine-disrupters found in plastic water and beverage bottles and plastic storage containers and thus can contaminate the food and drinks we consume.[3]

Benzene and toluene are volatile organic compounds (VOCs). Benzene is found in gasoline and cleaning products and is used in the production of plastics, resins, synthetic fibers, rubber lubricants, dyes, detergents, drugs, and pesticides. Living near a highway and therefore breathing in vehicle exhaust is associated with benzene exposure. Forest fires also release benzene into the environment.[4] This means a significant portion of the population in the Western U.S. is exposed to benzene every summer and fall,

| Toxin | Possible Sources of Exposure |
|---|---|
| Phthalates | Wall coverings, tablecloths, floor tiles, furniture upholstery, shower curtains, garden hoses, swimming pool liners, rainwear, baby pants, dolls, some toys, shoes, automobile upholstery and tops, food packaging, sheathing for wire and cable, medical tubing, blood storage bags, carpets, paints, glue, insect repellents, hair spray, nail polish, rocket fuel, carpet back coating, floor tile, adhesives, cosmetics, pesticides, toothbrushes, automobile parts, tools, toys, and aspirin. |
| Benzene | Pesticides, wildfire smoke, plastics, resins, synthetic fibers, rubber lubricants, dyes, detergents, drugs, vehicle exhaust, ground water. |
| Toluene | Paint thinners, paintbrush cleaners, nail polish, glues, inks, stain removers, vehicle exhaust, cigarette smoke, and groundwater. |
| Parabens | Personal care products such as soap, shampoo, cosmetics, and perfume. |
| Styrene | Cigarette smoke, packaging, household, and building products, vehicle exhaust, emissions from copy machines. |

due to exposure to wildfire smoke released from wildfires burning for weeks at a time. Toluene is another common environmental toxin. It can be found in paint thinners, paintbrush cleaners, nail polish, glues, inks, stain removers, and groundwater. Exposure also occurs when breathing in car exhaust and cigarette smoke.[5]

## Environmental Toxins and Alzheimer's

There is a scarcity of evidence associating parabens with Alzheimer's. Most of the reports in the medical literature involve parabens and autism (see below). The role of phthalates in Alzheimer's has also not been widely studied but justification exists that they may be implicated in the disorder. Phthalates have been shown to cross the blood-brain barrier.[6] Studies have also shown that phthalates interfere with neuroplasticity. In animal models, exposure to phthalates diminished dendritic spine density, neurogenesis, synaptogenesis and brain derived neurotrophic factor (BDNF) expression.[7,8,9] Furthermore, phthalates are estrogenic endocrine disrupters. Brain cells and neural circuits are likely impacted by phthalates because they need estrogens to function.[10]

Other evidence supports a potential role of phthalates in Alzheimer's. A cross-sectional epidemiological study utilized data from NHANES 2011-2012.[11] The study found that people with memory problems who had difficulties concentrating had greater levels of urinary phthalates along with other estrogenic chemicals.

Another study found that exposure to phthalates in the perinatal period reduced cognitive function and increased levels of phospho-Tau, an Alzheimer's disease precursor.[12] This study also determined that phthalates can impair the expression of insulin and an insulin-signaling pathway

in the hippocampus. Insulin resistance has been associated with the development of Alzheimer's disease.

Benzene and toluene have also been shown to have adverse effects on the brain. In a case control study, 193 probable Alzheimer's cases were compared to 243 controls free of dementia.[13] Exposure to benzene and toluene was associated with the onset of Alzheimer's disease. Furthermore, animal studies have shown that toluene exposure can lead to morphological changes in neurons.[13] When damage caused by toxins like toluene is combined with age-related damage to the brain, it can increase the vulnerability to Alzheimer's disease.[13] Exposure to toxins may accelerate the formation of plaques and neurofibrillary tangles.[13]

## Environmental Pollutants, Autism, and ADHD

Many of the toxins mentioned above have also been implicated in autism and/or attention deficit hyperactivity disorder (ADHD). Rat offspring that were exposed prenatally to butyl paraben suffered from neurodevelopmental disorders including anxiety and learning disabilities as adults.[14]

In another rodent study, the damaging effects of paraben exposure were found to mimic brain autism markers such as oxidative stress, decreased reduced glutathione levels and elevated oxidized glutathione, mitochondrial dysfunction and reduced levels of ATP, neuroinflammation, and elevated proinflammatory cytokine levels in the brain.[15]

A study by Ali and Elogy achieved similar findings. The evidence indicated that the social, learning, and memory behavioral deficits in rats with autism were similar to the adverse effects that occurred when rats were exposed to butyl paraben prenatally and for 21 days postnatally.[16] Additionally, there were similarities between monoamine content, amino acids, and BDNF in the autistic rats and in offspring exposed to butyl paraben in comparison with the controls.

In a human study of 328 inner-city mothers and their children, prenatal maternal exposure to di-n-butyl phthalate (DnBP) and di-isobutyl phthalate (DiBP) was inversely associated with child IQ at seven years of age.[17] A significant inverse correlation was also found between maternal prenatal metabolite levels of DnBP and DiBP and child processing speed, perceptual

reasoning, and working memory. DiBP levels were associated with reduced child verbal comprehension and butylbenzyl phthalate (BBzP) levels were linked to lower child perceptual reasoning.

Another study investigated whether there was an association between exposure to estrogenic endocrine disrupting chemicals such as phthalates and autism and ADHD.[18] The study indicated intracranial exposure to several classes of these chemicals including phthalates led to pronounced hyperactivity in neonatal rats.

Larsson and colleagues conducted a retrospective study of young children. Autism spectrum disorder was more common in the children exposed to phthalates from PVC pipe dust.[19] Miodovnik and associates achieved similar results in a human study that found higher maternal urinary phthalate levels correlated with adverse neurobehavioral outcomes including increased social deficits and poorer social cognition, social communication, and social awareness in the adolescent offspring.[20] In another study, Polish researchers measured 11 phthalate metabolites in the urine from mothers during the third trimester of pregnancy and from their children at two years of age.[21] Prenatal phthalate exposure was associated with worse child psychomotor development.

Exposure to benzene and other air pollutants has also been associated with impaired intestinal permeability, a problem commonly found in children with autism spectrum disorder or ADHD.[22] Exposure to benzene and other air pollutants damages epithelial and endothelial barriers and affects tight junction proteins and neural antibodies.[22] Tight junction antigens to "self" can result in an autoimmune response that may lead to neuroinflammation.[22]

Styrene is another toxin linked to childhood neurological disorders. During pregnancy, mothers who live in areas with higher levels of styrene in the air have an increased risk of having children with autism.[23]

## Amyotrophic Lateral Sclerosis, Parkinson's Disease, and Other Neurological Disorders

Volatile organic compounds such as toluene have been found to trigger the development of Amyotrophic Lateral Sclerosis (ALS).[24] Toluene's role in the etiology of this disorder includes the disruption of motor function and elevated oxidative stress.[24] Benzene-derived pesticides have also been found in higher levels in people with Parkinson's disease compared with healthy controls.[25] Furthermore, many genes influenced by estrogenic endocrine disrupters such as phthalates play a role in brain diseases such as Parkinson's disease, Huntington's disease, ALS, autism spectrum disorder, Alzheimer's disease, and brain neoplasms.[10]

## The Critical Importance of Testing for Environmental Pollutants

There's an abundance of research showing the damaging effects of environmental toxins on today's children. In addition, the autism prevalence has reached 1 in 59 children.[26] Knowing this statistic, doesn't it make sense to test for environmental pollutants before conceiving? Due to the wide net toxins like phthalates, parabens, benzene, styrene, and toluene cast over everyone's health, testing all patients for environmental pollutants is a savvy approach to resolving an important underlying cause of disease.

## References:


1 Boberg J, Taxvig C, Christiansen S, Hass U. Possible endocrine disrupting effects of parabens and their metabolites. *Reprod Toxicol.* 2010 Sep;30(2):301-12.

2 Manivannan Y, Manivannan B, Beach TG, Rolf U. Role of Environmental Contaminants in the Etiology of Alzheimer's Disease: A Review. *Curr Alzheimer Res.* 2015 Feb;12(2):116-46.

3 Halden RU. Plastics and health risks. *Annu Rev Public Health.* 2010;31:179-94.

4 https://www.dhs.wisconsin.gov/chemical/benzene.htm Accessed March 5, 2019

5 https://www.dhs.wisconsin.gov/chemical/toluene.htm Accessed March 5, 2019

6 Szychowski KA, Wójtowicz AK. [Components of plastic disrupt the function of the nervous system]. [Article in Polish] *Postepy Hig Med Dosw* (Online). 2013 May 27;67:499-506.

7 Smith CA, Holahan MR. Reduced hippocampal dendritic spine density and BDNF expression following acute postnatal exposure to di(2-ethylhexyl) phthalate in male Long Evans rats. *PLoS One.* 2014 Oct 8;9(10):e109522.

8 Holahan MR, Smith CA. Phthalates and neurotoxic effects on hippocampal network plasticity. *Neurotoxicology.* 2015 May;48:21-34.

9 Li XJ, Jiang L, Chen L, et al. Neurotoxicity of dibutyl phthalate in brain development following perinatal exposure: a study in rats. *Environ Toxicol Pharmacol.* 2013 Sep;36(2):392-402.

10 Preciados M, Yoo C, Roy D. Estrogenic Endocrine Disrupting Chemicals Influencing NRF1 Regulated Gene Networks in the Development of Complex Human Brain Diseases. *Int J Mol Sci.* 2016 Dec 13;17(12). pii: E2086.

11 Shiue I. Arsenic, heavy metals, phthalates, pesticides, hydrocarbons and polyfluorinated compounds but not parabens or phenols are associated with adult remembering condition: US NHANES, 2011-2012. *Environ Sci Pollut Res Int.* 2015 Apr;22(8):6381-6.

12 Sun W, Ban JB, Zhang N, et al. Perinatal exposure to Di-(2-ethylhexyl)-Phthalate leads to cognitive dysfunction and phospho-tau level increase in aged rats. *Environ Toxicol.* 2014 May;29(5):596-603.

13 Kukull WA, Larson EB, Bowen JD, et al. Solvent exposure as a risk factor for Alzheimer's disease: a case-control study. *Am J Epidemiol.* 1995 Jun 1;141(11):1059-71; discussion 1072-9.

14 Kawaguchi M, Irie K, Morohoshi K, et al. Maternal isobutyl-paraben exposure alters anxiety and passive avoidance test performance in adult male rats. *Neurosci Res.* 2009 Oct;65(2):136-40.

15 Hegazy HG, Ali EH, Elgoly AH. Interplay between pro-inflammatory cytokines and brain oxidative stress biomarkers: evidence of parallels between butyl paraben intoxication and the valproic acid brain physiopathology in autism rat model. *Cytokine*. 2015 Feb;71(2):173-80.

16 Ali EH, Elgoly AH. Combined prenatal and postnatal butyl paraben exposure produces autism-like symptoms in offspring: comparison with valproic acid autistic model. *Pharmacol Biochem Behav*. 2013 Oct;111:102-10.

17 Factor-Litvak P, Insel B, Calafat AM, et al. Persistent Associations between Maternal Prenatal Exposure to Phthalates on Child IQ at Age 7 Years. *PLoS One*. 2014 Dec 10;9(12):e114003.

18 Masuo Y, Morita M, Oka S, Ishido M. Motor hyperactivity caused by a deficit in dopaminergic neurons and the effects of endocrine disruptors: a study inspired by the physiological roles of PACAP in the brain. *Regul Pept*. 2004 Dec 15;123(1-3):225-34.

19 Larsson M, Weiss B, Janson S, et al. Associations between indoor environmental factors and parental-reported autistic spectrum disorders in children 6-8 years of age. *Neurotoxicology*. 2009 Sep;30(5):822-31.

20 Miodovnik A, Engel SM, Zhu C, et al. Endocrine disruptors and childhood social impairment. *Neurotoxicology*. 2011 Mar;32(2):261-7.

21 Polanska K, Ligocka D, Sobala W, Hanke W. Phthalate exposure and child development: the Polish Mother and Child Cohort Study. *Early Hum Dev*. 2014 Sep;90(9):477-85.

22 Calderón-Garcidueñas L, Vojdani A, Blaurock-Busch E, et al. Air pollution and children: neural and tight junction antibodies and combustion metals, the role of barrier breakdown and brain immunity in neurodegeneration. *J Alzheimers Dis*. 2015;43(3):1039-58.

23 Carter CJ, Blizard RA. Autism genes are selectively targeted by environmental pollutants including pesticides, heavy metals, bisphenol A, phthalates and many others in food, cosmetics or household products. *Neurochem Int*. 2016 Oct 27. pii: S0197-0186(16)30197-8. [Epub ahead of print]

24 Ratner MH, Jabre JF, Ewing WM, et al. Amyotrophic lateral sclerosis-A case report and mechanistic review of the association with toluene and other volatile organic compounds. *Am J Ind Med*. 2018 Mar;61(3):251-60.

25 Richardson JR, Shalat SL, Buckley B, et al. Elevated serum pesticide levels and risk of Parkinson disease. Arch Neurol. 2009 Jul;66(7):870-5.

26 https://www.autismspeaks.org/science-news/cdc-increases-estimate-autisms-prevalence-15-percent-1-59-children Accessed March 5, 2019