

Environmental Influences in ASD and Essential Preconception Advice

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Disclaimer

While Dr. Ahsan has attempted to make the information in this presentation as accurate as possible, the information is provided without any expressed or implied warranty. The purpose of this lecture is to provide information about the evaluation and treatment of environmental risk factors in autism and other conditions. Please be advised that Dr. Ahsan is not giving medical advice and that circumstances may dictate different treatments. Any reviewed treatments in this lecture are considered off-label and not FDA approved. Before beginning any treatment, please consult with your child's physician.

The use of every treatment in autism is "off-label" except for Risperidone and Aripiprazole for the treatment of irritability.



Toxins and Neurodevelopmental Disorders

A few industrial chemicals (e.g., lead, methylmercury, polychlorinated biphenyls [PCBs], arsenic, and toluene) are recognized causes of neurodevelopmental disorders and subclinical brain dysfunction. Exposure to these chemicals during early fetal development can cause brain injury at doses much lower than those affecting adult brain function.

Grandjean et al, 2006 Lancet 368:2167-2178

Since 2006, epidemiological studies have documented six additional developmental neurotoxicants—**manganese, fluoride, chlorpyrifos, dichlorodiphenyltrichloroethane (DDT), tetrachloroethylene (organic solvent), and the polybrominated diphenyl ethers (PBDEs- flame retardants).** We postulate that even more neurotoxicants remain undiscovered.

Grandjean et al, Lancet Neurology 2014: 13:330-338

Toxins and Autism

A comprehensive literature search has implicated several environmental factors associated with the development of ASD. These include **pesticides, phthalates, polychlorinated biphenyls, solvents, air pollutants, fragrances, glyphosate and heavy metals, especially aluminum used in vaccines as adjuvant**. Importantly, the majority of these toxicants are some of the most common ingredients in cosmetics and herbicides to which almost all of us are regularly exposed to in the form of fragrances, face makeup, cologne, air fresheners, food flavors, detergents, insecticides and herbicides.

Sealy et al, 2016 Environment International 88: 288-298

Toxins and Autism

Toxicants implicated in ASD included:

- **pesticides**
- **phthalates**
- **polychlorinated biphenyls (PCBs)**
- **solvents**
- **toxic waste sites**
- **air pollutants**
- **heavy metals**

Strongest evidence found for air pollutants and pesticides.

Rossignol et al *Transl Psychiatry*. 2014;4:e360

Body Burden

The Environmental Working Group, July 14, 2005

“In a study spearheaded by the Environmental Working Group (EWG) in collaboration with Commonweal, **researchers at two major laboratories found an average of 200 industrial chemicals and pollutants in umbilical cord blood from 10 babies born** in August and September of 2004 in U.S. hospitals. Tests revealed a total of 287 chemicals in the group. Among them are eight perfluorochemicals used as stain and oil repellants in fast food packaging, clothes and textiles — including the Teflon chemical PFOA, recently characterized as a likely human carcinogen by the EPA's Science Advisory Board — dozens of widely used brominated flame retardants and their toxic by-products; and numerous pesticides.

Of the 287 chemicals we detected in umbilical cord blood, we know that **180 cause cancer in humans or animals, 217 are toxic to the brain and nervous system, and 208 cause birth defects or abnormal development in animal tests.**”

CHEMICALS AND POLLUTANTS DETECTED IN HUMAN UMBILICAL CORD BLOOD	
Hg	Mercury (Hg) - tested for 1, found 1 Pollutant from coal-fired power plants, mercury-containing products, and certain industrial processes. Accumulates in seafood. Harms brain development and function.
PAH	Polyaromatic hydrocarbons (PAHs) - tested for 18, found 9 Pollutants from burning gasoline and garbage. Linked to cancer. Accumulates in food chain.
BD/F	Polybrominated dibenzodioxins and furans (PBDD/F) - tested for 12, found 7 Contaminants in brominated flame retardants. Pollutants and byproducts from plastic production and incineration. Accumulate in food chain. Toxic to developing endocrine (hormone) system
PFC	Perfluorinated chemicals (PFCs) - tested for 12, found 9 Active ingredients or breakdown products of Teflon, Scotchgard, fabric and carpet protectors, food wrap coatings. Global contaminants. Accumulate in the environment and the food chain. Linked to cancer, birth defects, and more.
D/F	Polychlorinated dibenzodioxins and furans (PCDD/F) - tested for 17, found 11 Pollutants, by-products of PVC production, industrial bleaching, and incineration. Cause cancer in humans. Persist for decades in the environment. Very toxic to developing endocrine (hormone) system.
OC	Organochlorine pesticides (OCs) - tested for 28, found 21 DDT, chlordane and other pesticides. Largely banned in the U.S. Persist for decades in the environment. Accumulate up the food chain, to man. Cause cancer and numerous reproductive effects.
PBDE	Polybrominated diphenyl ethers (PBDEs) - tested for 46, found 32 Flame retardant in furniture foam, computers, and televisions. Accumulates in the food chain and human tissues. Adversely affects brain development and the thyroid.
CN	Polychlorinated Naphthalenes (PCNs) - tested for 70, found 50 Wood preservatives, varnishes, machine lubricating oils, waste incineration. Common PCB contaminant. Contaminate the food chain. Cause liver and kidney damage.
PCB	Polychlorinated biphenyls (PCBs) - tested for 209, found 147 Industrial insulators and lubricants. Banned in the U.S. in 1976. Persist for decades in the environment. Accumulate up the food chain, to man. Cause cancer and nervous system problems.

Effects of Chemical and Metal Toxins

- Inhibit mitochondrial function
- Deplete glutathione
- Contribute to immune dysregulation
- Increase oxidative stress
- Inhibit thyroid function
- Increase glutamate excitotoxicity
- Cause inflammation

Many of these are physiologic abnormalities seen in individuals with ASD

Rossignol et al *Transl Psychiatry*. 2014;4:e360

Gene Toxicant Interactions in ASD

- Several studies have reported that some individuals with ASD express polymorphisms in genes involved in the detoxification of environmental pollutants.
- More than 100 such genes, termed '**environmental response genes**' may contribute to ASD risk
- Single Nucleotide polymorphisms (SNPs) in environmental response genes are believed to increase susceptibilities to the adverse effects of environmental toxicants

Rossignol et al *Transl Psychiatry*. 2014;4:e360

Gene Toxicant Interactions in ASD

Environmental Response Genes Potentially Implicated in ASD

- **Paraoxonase (PON1)** – enzyme that hydrolyzes and inactivates many pesticides
- **Glutathione S-transferases (GSTM1 and GSTP1)** – catalyze the detoxification of heavy metals and xenobiotic compounds
- **Delta aminolevulinic acid dehydratase (ALAD2)** – associated with increased susceptibility to lead toxicity and cognitive impairments from lead exposure
- **Divalent metal ion transporter (SCL11A3) & metal regulatory transcription factor 1 (MTF1)** – important in heavy metal metabolism

Rossignol et al *Transl Psychiatry*. 2014;4:e360

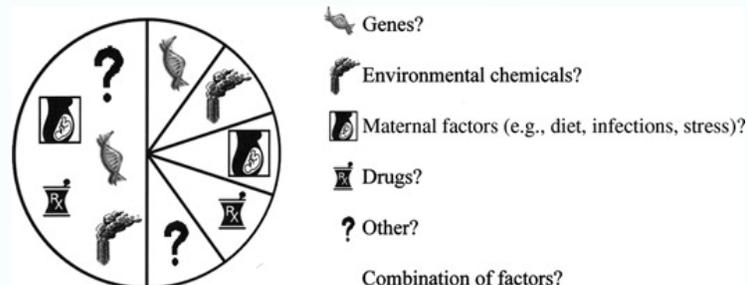


Fig. 1. The pie chart illustrates the most likely risk factors for autism. At issue is the way in which these factors act either independently and/or through various interactions to produce autism. To date, much of this remains to be determined.

Dietert et al., (2017) Environmental risk factors for autism, *Emerging Health Threats Journal*, 4:1

Male Susceptibility to Toxins

Male to female ratio in ASD is 4:1

Boys more likely to be affected by toxic metals, pesticides, and PCBs due to:

- Lower glutathione levels
- Higher oxidative stress
- Excrete mercury less readily (retain more)
- Estrogen is an anti-oxidant
- Testosterone may increase toxicity of mercury

Male-related hormonal factors may increase adverse effects of toxins and contribute to higher male:female ratio in ASD

Rossignol et al *Transl Psychiatry*. 2014;4:e360

Air Pollution



BAD AIR: U.S. pollution levels have come way down since the 1970s, but there's still enough smog to raise the risk for cardiovascular deaths. **Researchers are also drawing new connections between dirty air and metabolic and brain disorders.**

<https://www.sciencenews.org/article/list-diseases-linked-air-pollution-growing>

Air Pollution

Top Pollutants

Ammonia
Carbon Monoxide
Fine particulates
Lead
Nitrogen oxides
Sulfur dioxide
Volatile organic compounds

Pollutant Sources

Agriculture
Dust
Fuel
Industrial
Miscellaneous
Solvent
Vegetation
Vehicles

Traffic-Related Air Pollution, Particulate Matter, and Autism

Volk, et al. *JAMA Psychiatry*. 2013;70(1):71-77

Study examined the relationship between traffic-related air pollution, air quality, and autism

Findings: **Children with autism were more likely to live at residences that had the 1) highest exposure to traffic-related air pollution 2) higher regional measures of nitrogen dioxide, and 3) particulate matter less than 2.5 μ m and 10 μ m (PM_{2.5} and PM₁₀) diameter during gestation and during first year of life.**

Air Pollution and Autism

Six retrospective case-controlled studies examined ASD risk and estimated **exposure to air pollution during gestation and found an association between ASD and air pollution.**

Three retrospective case-controlled showed an association with ASD and air pollution in children with ASD.

Rossignol et al *Transl Psychiatry*. 2014;4:e360

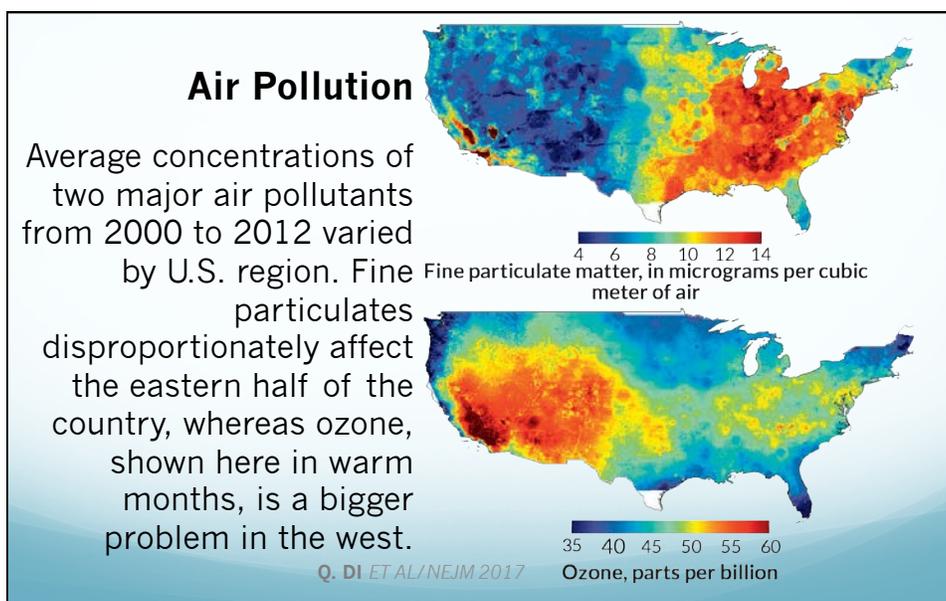
Autism Spectrum Disorder and Particulate Matter Air Pollution before, during, and after Pregnancy: A Nested Case–Control Analysis within the Nurses’ Health Study II Cohort

Objective: We explored the association between maternal exposure to particulate matter (PM) air pollution and odds of ASD in her child.

Results: PM_{2.5} exposure during pregnancy was associated with increased odds of ASD...

Conclusions: **Higher maternal exposure to PM_{2.5} during pregnancy, particularly the third trimester, was associated with greater odds of a child having ASD**

Raz et al, 2015 *Environmental Health Perspectives* 123(3): 264-270



A cleanroom sleeping environment's impact on markers of oxidative stress, immune dysregulation, and behavior in children with autism spectrum disorders

- Cleanroom is controlled environment where High Efficiency Particulate Air (HEPA) filter or Ultra Low Particulate Air (ULPA) filters are used to control number of particles and particle size in the room
 - therefore has extremely low level of pollutants like dust, airborne microbes, aerosol particles, and chemical vapors.
- Study evaluated the physiological and behavioral effects of children with autism sleeping in a Class 5 cleanroom.
- Evaluated changes in toxin levels, oxidative stress, immune dysregulation, and behavior.
- **Improvements were seen in oxidative stress and immune-related markers as well as behavior.**

Faber S et al, *BMC*. 2015;15:71

Pesticides



Pesticides

Children of **mothers living near agriculture organochlorine pesticide applications had increased odds ratio for ASD of 6.1**. ASD risk increased with the poundage of pesticide applied and decreased with distance from field sites.

Roberts et al, Environ Health Perspect. 2007; 115: 1482-9

Study following inner-city newborn **infants who had prenatal exposure to organophosphate insecticide chlorpyrifos** found that children with higher estimated exposure levels of chlorpyrifos were **more likely to develop symptoms of PDD by 36 months of age**.

Rauh et al, Pediatrics; 118: e1845-e1859

Pesticides

Three studies reported an association between pesticides exposure during childhood and ASD. Evidence linking pesticide exposure in ASD does not appear to be as strong during childhood as during gestation, but need more studies for childhood exposure.

Rosignol et al *Transl Psychiatry*. 2014;4:e360

Indoor Pesticides Sources

Brought in from outdoors (e.g.. pesticides used for lawn care, school playgrounds, school sports' fields, drift from agriculture)

Used in varnishes, colors, adhesives

Used in finishing textiles, leather, carpets

Insect sprays

Bait boxes

Pest Strips

Pesticide Pet Sprays (e.g.. to kill fleas and ticks)

Bug bombs/foggers

Pesticide Pet Shampoos

Pesticides in Food

American Academy of Pediatrics Policy Statement –
Council on Environmental Health, Pediatrics,
December 2012, Volume 130/ Issue 6

“For many children, **diet may be the most influential source**, as illustrated by an intervention study that placed children on an organic diet (produced without most conventional pesticides) and observed drastic and immediate decrease in urinary excretion of organophosphate pesticide metabolites.”

Organic Diets Significantly Lower Children’s Exposure to Organophosphorus Pesticides.

- Study Substituted children’s conventional diets **with organic food items for 5 consecutive days** and measured dietary organophosphorus exposure in elementary school-age children through urinary biomonitoring.
- Found that the **median urinary concentrations of the specific metabolites for malathion and chlorpyrifos decreased to the nondetectable levels immediately after the introduction of organic diets and remained nondetectable** until the conventional diets were reintroduced.
- Median concentrations **for other organophosphorus pesticide metabolites were also lower in the organic diet consumption days**

Lu et al., Environmental Health Perspectives 2006;114(2):260–263

Organic Diets Significantly Lower Children's Exposure to Organophosphorus Pesticides.

- Conclusion: **that an organic diet provides a dramatic and immediate protective effect against exposures to organophosphorus pesticides** that are commonly used in agricultural production.
- Also concluded that these **children were most likely exposed to these organophosphorus pesticides exclusively through their diet.**
- First study to employ a longitudinal design with a dietary intervention to assess children's exposure to pesticides. Provides new and persuasive evidence of the effectiveness of this intervention.

Lu et al., Environmental Health Perspectives 2006;114(2):260–263

Environmental Working Group's 2019 Shopper's Guide to Pesticides in Produce

Dirty Dozen

1. Strawberries
2. Spinach
3. Kale
4. Nectarines
5. Apples
6. Grapes
7. Peaches
8. Cherries
9. Pears
10. Tomatoes
11. Celery
12. Potatoes

**Hot Peppers – contain traces of highly toxic pesticides

Clean Fifteen

- | | |
|----------------------|---------------|
| 1. Avocados | 13. Broccoli |
| 2. Sweet Corn | 14. Mushrooms |
| 3. Pineapples | 15. Honeydew |
| 4. Sweet Peas Frozen | Melons |
| 5. Onions | |
| 6. Papayas | |
| 7. Eggplants | |
| 8. Asparagus | |
| 9. Kiwis | |
| 10. Cabbage | |
| 11. Cauliflower | |
| 12. Cantaloupes | |

From EWG Shopper's Guide to Pesticides in Produce www.foodnews.org

Water



Drinking Water

Drinking water for more than 170 million Americans contains **radioactive elements including radium, radon, and uranium** at levels that may increase the risk of cancer, according to an EWG analysis of 2010 to 2015 test results from public water systems nationwide. By far the most widespread are two isotopes of radium known as **radium-226 and radium-228, which contaminate tap water in every state.**

Environmental Working Group, January 11, 2018

Drinking Water

Carcinogenic Chemical Chromium-6 (i.e.. chemical Erin Brockovich crusaded against in tap water in Hinkley, CA) was found to contaminate water supplies for more than 200 million Americans in all 50 states. This was an EWG analysis of federal data from nationwide drinking water tests. Chromium-6 can cause lung cancer, liver damage, reproductive problems, and **developmental harm**. Risks are greater with certain groups – **infants and children**, people taking antacids, people with poorly functioning livers.

Environmental Working Group, September 20, 2016

Drinking Water

Lead, arsenic, mercury, and other contaminants were found in tap water by local water utility tests in EWG's recently released national drinking water database.

- Lead and mercury – highly potent neurotoxins that can cause serious nervous system damage in children
- Arsenic – known carcinogen and common drinking water contaminant

Data from almost 50,000 utilities showed that **arsenic contaminates more than 7,230 water supplies serving 70 million people** and that **mercury contaminates more than 280 water supplies serving 2.5 million people**. Almost 19,000 public water systems in all 50 states had at least one detection of lead above the level at which a formula-fed baby is at risk.

Environmental Working Group, August 15, 2017

COMPREHENSIVE DRINKING WATER ANALYSIS				
		WATER TYPE: Municipal ORDERED BY: Salma Ahsan 7860 Glisten Ave Sandy Springs, GA 30328 USA	LAB NUMBER: W170113-2403-1 DATE ORDERED: 01/13/2017 DATE COLLECTED: 01/21/2017 DATE COMPLETED: 02/10/2017	
PRIMARY EPA DRINKING WATER METALS				
PRIMARY METALS	RESULT parts per billion (ppb)	ACCEPTABLE	CAUTION	UNACCEPTABLE
Arsenic (As)	< 1	X		
Copper (Cu)	38	X		
Lead (Pb)	0.6		X	
Thallium (Tl)	< 0.1	X		
Uranium (U238)	< 1	X		
Antimony (Sb)	< 0.5	X		
Barium	12	X		
Beryllium	< 0.4	X		
Cadmium (Cd)	< 1	X		
Chromium (Cr)	< 10	X		
Mercury (Hg)	< 0.5	X		
Nickel (Ni)	< 5	X		
Selenium (Se)	< 10	X		
The EPA has not established levels for this category				
SECONDARY EPA DRINKING WATER METALS				
SECONDARY METALS	RESULT parts per billion (ppb)	ACCEPTABLE	CAUTION	UNACCEPTABLE
Aluminum (Al)	< 10	X		
Iron (Fe)	< 30	X		
Manganese (Mn)	< 5	X		
Zinc (Zn)	< 50	X		
The EPA has not established levels for this category				
FLUORIDE				
	RESULT parts per million (ppm)	ACCEPTABLE	CAUTION	UNACCEPTABLE
Fluoride (F ⁻)	0.6	X		
The EPA has not established levels for this category				

Heavy Metals

- Seven studies reported possible relationship between autism severity and biomarkers of heavy metals_(e.g.. mercury, lead, cadmium, aluminum, arsenic, etc.)
 - Dose-effect relationship
- Twelve studies reported improvements in biomarkers of toxicants or in clinical symptoms in children with ASD using treatments incorporating detoxification methods
 - No significant adverse effects reported
- None of the studies contained a control group or were placebo controlled

Rossignol et al *Transl Psychiatry*. 2014;4:e360

Lead

“Blood lead concentrations, even those below 10 µg per deciliter, are inversely associated with children’s IQ scores at three and five years of age, and associated declines in IQ are greater at these concentrations than at higher concentrations. These findings suggest that more U.S. children may be adversely affected by environmental lead than previously estimated.”

- IQ declined by 7.4 points as lifetime average blood lead concentrations increased from 1 to 10 µg per deciliter.

Canfield et al, The New England Journal of Medicine, 2003; 348:1517-26

Lead

Higher Blood Lead levels were correlated with lower intellectual functioning in children with ASD

Campbell, et al, J Am Acad Child Psychiatry 1980; 19: 193-212

From EPA: the maximum contaminant level goal (MCLG) for lead is zero. EPA has set this level based on the best available science which shows **there is no safe level of exposure to lead.**

<https://www.epa.gov/ground-water-and-drinking-water/basic-information-about-lead-drinking-water#regs>

Mercury

- Most toxic nonradioactive element on the planet
- Mercury in dental amalgams

Ingestion may cause death. ‡
Neurotoxic/Nephrotoxic
Inhalation can cause
Bronchiolitis, Pneumonitis
Pulmonary Edema
Irritant sensitizer to skin
and eyes, acute exposure
may cause redness and
irritation.
Possible visual disturbances.
Keep out of reach of children.
Not for food or drug use



HENRY SCHEIN®
Dental Mercury
Triple Distilled Quality
99.9995+%

"This product appears on the American Dental Association List of Certified Dental Materials."

See MSDS before handling this product.

California Prop 65 Warning:
This product contains mercury, a chemical known to the State of California to cause birth defects or other reproductive harm.

1lb (0.453 kg)

101-7570
Hazard Warning



"Harmful if vapors are inhaled"
"Avoid breathing, keep container closed, use with adequate ventilation"

CORROSIVE



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Mercury in Fish

No fish completely free of mercury and other pollutants

The lists below clearly show that virtually all fish have problems with accumulated toxins.

High Mercury Seafood	Intermediate Mercury Seafood	Low Mercury Seafood	High PCBs and Other Pollutants
King Shark Whale Swordfish Tilefish Grouper Sea Bass Marlin Halibut Lobster Scorpionfish Snapper	Tuna Pike Largemouth Bass Bluefish Carp Mahimahi Mackerel (Gulf) Monkfish Orange Roughy Cod Croaker Polluck Whitefish Sea Trout (Weakfish)	Shrimp Tilapia Haddock Scallops Squid Trout Hake Ocean Perch	Mackerel Salmon Sardines Herring Bluefish Lobster Catfish Clams Oysters Crab
			<i>Source:</i> FDA Surveys 1990-2003

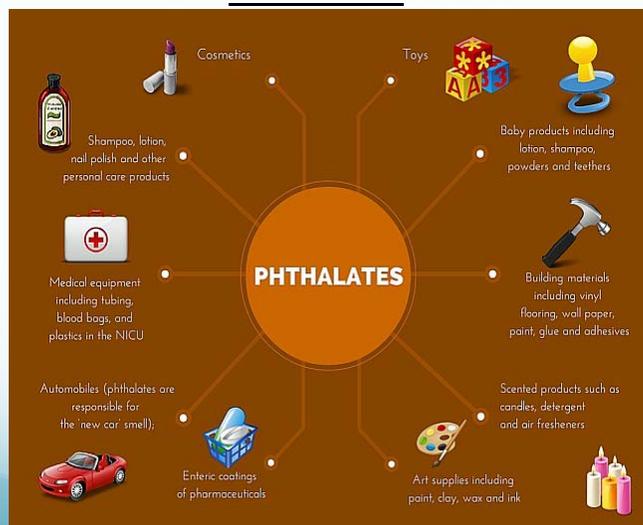
High Fructose Corn Syrup

Study Finds High Fructose Corn Syrup Contains Mercury

The Washington Post, January 26, 2009

“Almost half of tested samples of commercial high-fructose corn syrup (HFCS) contained mercury.....HFCS has replaced sugar as the sweetener in many beverages and foods such as breads, cereals, breakfast bars, lunch meats, yogurts, soups and condiments. On average, Americans consume about 12 teaspoons per day of HFCS, but teens and other high consumers can take in 80 percent more HFCS than average. “Mercury is toxic in all its forms. Given how much high-fructose corn syrup is consumed by children, it could be a significant additional source of mercury never before considered. We are calling for immediate changes by industry and the [U.S. Food and Drug Administration] to help stop this avoidable mercury contamination of the food supply,” the Institute for Agriculture and Trade Policy’s Dr. David Wallinga, a co-author of both studies, said in a prepared statement.

Phthalates



Phthalates

- Phthalates are esters of phthalic acid and are used to soften plastic polymers
- **Found in hundreds of products including soft vinyl plastic toys, shampoos, hair sprays (to decrease stiffness), nail polish (to prevent chipping), cosmetics, waxed cheese wraps, perfumes and deodorants (to keep the smells), new cars, pharmaceuticals, etc.**
- **Cause oxidative stress; stimulate inflammatory markers**
Toxicol Appl Pharmacol 2008 Sept 1: 231 (2): 241-7
- Study of 48 children with ASD and 45 control children reported that **urinary concentrations of two phthalates were significantly increased in the ASD group** compared with the control
Testa et al, ASN Neuro 2012; 4: 223-229

Reducing Phthalate, Paraben, and Phenol Exposure from Personal Care Products in Adolescent Girls: Findings from the HERMOSA Intervention Study

- Personal care products are a source of exposure to potentially endocrine-disrupting chemicals such as phthalates, parabens, triclosan, and benzophenone-3 (BP-3) for adolescent girls.
- Results: The adolescent girls in this study experienced an average within-girl **decline of 27-45% in urinary concentrations** of certain phthalates, certain parabens, triclosan, and oxybenzone **after 3 days of abstaining from conventional personal care products**
- **Choosing personal care products that are labeled to be free of phthalates, parabens, triclosan, and BP-3, can reduce personal exposure to possible endocrine-disrupting chemicals.**

Harley et al. 2016 Environmental Health Perspectives 124(10): 1600-1607

Polyvinyl Chloride

- Comes in two forms, rigid and flexible
 - Rigid form used in construction for pipes, doors, windows, non-food packaging, cards, flooring (e.g.. vinyl siding, vinyl flooring), etc.
 - PVC flooring is a source of airborne phthalates
 - Flexible form made by adding plasticizers like phthalates
- Uses of Flexible PVC:
 - Insulation of electrical cables
 - Clothing (e.g.. water resilient coats, shoes, sports bags, etc. apparel)
 - **Healthcare** (e.g.. catheters, blood containing bags, ostomy products, hemodialysis sets, etc.)
- **This study showed PVC flooring material, in comparison to wood flooring, located in parent's room or child's room was associated with an increased risk of ASD**



Larsson, et al., Neurotoxicology 2009; 30: 822-831

Polybrominated Diphenyl Ethers (PBDEs)

Brominated hydrocarbons that are used as **Fire Retardants**

Used in:

- Polyurethane foam
- Children's clothing – especially children's sleepwear
- Cell phones
- Electronics
- Insulation in Buildings
- Computers
- Televisions
- Textiles
- Many more



Polybrominated Diphenyl Ethers (PBDEs)

- Adverse Health Effects include:
 - Thyroid hormone disruption
 - Permanent learning and memory impairments
 - Behavioral changes
 - Hearing deficits
 - Delayed puberty onset
 - Decreased sperm count
 - Fetal malformations
 - Cancer
- **Metabolic Impact of PBDEs**
 - **Damage Mitochondria**
 - **GABA dysregulation**
 - **Glutamate dysregulation**
 - **Glutathione dysregulation**

Polybrominated diphenyl ether (PBDE) flame retardants as potential autism risk factors

Brominated flame retardants, including Polybrominated diphenyl ethers (PBDEs) have been used at increasing levels in home furnishings and electronics over the past 25 years. They have also become widespread environmental pollutants. High PBDE levels have been detected in food, household dust, and indoor air, with subsequent appearance in animal and human tissues. This minireview summarizes studies on the extent to which these compounds can act as potent thyroid hormone mimetics, and emerging studies on long-term neurological effects of acute administration of PBDEs during development. **When these data are considered in combination with the extensive literature on stage-dependent effects of thyroid hormone on aspects of brain development that are also implicated in autistic brains, a hypothesis that PBDEs might also serve as autism risk factors emerges.** Studies designed to explicitly test this hypothesis will require chronic exposure paradigms, and specific body burden and behavioral monitoring in animal models. Such testing may help to prioritize extensive human epidemiological studies, as well as offer protocols for evaluation of future compounds.

Messer, *Physiol Behav* 2010 Jun1; 100(3):245-9

Polyurethane Foam

- Petroleum-derived synthetic material
- **Used in mattresses** because plush, durable, soft – cushions your body (**e.g.. memory foam**)
- **Highly flammable therefore need 20-30% flame retardants** by weight for regulations
- **Children's crib mattresses can be significant source of chemical contaminants**
 - Infant crib mattresses released nearly 30 different types of volatile organic compounds, or VOCs, and other potentially harmful airborne chemicals such as endocrine-disrupting phthalates and fragrance allergen



Boor et al, *Environ. Sci. Technol. Lett.*, 2015, 2 (4), pp 89–94

Other Toxins

Bisphenol A (BPA) – starting material for synthesis of plastics; found in plastics such as plastic bottles, baby bottles, water bottles, canned food, canned infant formula, dental sealants

Triclosan – antibacterial and antifungal found in soaps, shampoos, deodorants, toothpastes, cleaning supplies

- Could be contributing to severe food and environmental allergies in children

Other Toxins

PERC – perchloroethylene; **used in dry cleaning; male mice developed autistic like behaviors after gestational and postnatal exposure**

Perfluorinated Compounds (PFCs) – used as repellants as **makes products resistant to water and oil**; e.g.. used in nonstick cookware, furniture and rug stain repellant, rain jackets, *****fast food wrappers*****

- associated with cancer, reproductive problems, **birth and developmental defects**, and with immune system suppression

Biological Toxins: Mycotoxins

- Mycotoxins have toxicological effects, resembling several symptoms associated with autism such as oxidative stress, intestinal permeability, and inflammation.
- Study focused on a group of mycotoxins to test their role in the manifestation of autism
- Results: a **significant association was found for Ochratoxin A (OTA) levels in urine and serum in patients with autism versus controls**. Results are the first **describing a possible role of OTA in the pathobiology of autism**. OTA exerts its **neurotoxicity especially in males** in animal models.
- A personalized diet coupled with **probiotic administration, especially OTA adsorbing *Lactobacillus*, could ameliorate autistic symptoms in OTA-positive patients**.

Santis et al, (2017) Role of mycotoxins in the pathobiology of autism: A first evidence, Nutritional Neuroscience, DOI: [10.1080/1028415X.2017.1357793](https://doi.org/10.1080/1028415X.2017.1357793)

Reducing your Child's Toxic Load

- Air purifiers with HEPA filter, especially in the bedroom
- Vacuum cleaner with HEPA filter
- Eat organic, non GMO food
- Avoid farm raised fish and fish with high mercury content (e.g.. King mackerel, Marlin, Orange Roughy, Shark, Swordfish, Tilefish, Tuna, Bluefish, grouper, etc.)
- Take off shoes before coming into the home
- Avoid use of herbicides or pesticides on lawn, on pets
- Use carbon based water filters in home (reverse osmosis filter for under kitchen sink for drinking and cooking; filters on shower/sinks or whole home water filtration system)

Reducing your Child's Toxic Load

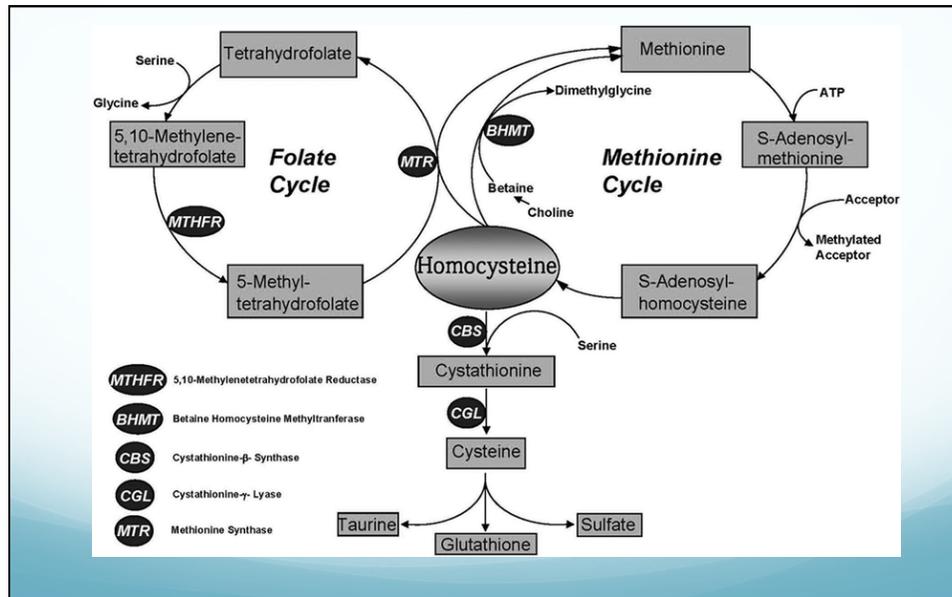
- Send your children to school with filtered water in glass or stainless steel bottles; tell your children and teachers/staff to not let them drink from the drinking fountains
- Never microwave food in plastic containers
- Avoid storing food in plastic containers; store food in glass or Pyrex
- Choose glass or wax box containers when purchasing beverages; take your own mug with you when buying coffee
- Avoid aluminum and non-stick cookware
 - Alternatives include: stainless steel, cast iron, ceramic titanium, porcelain enameled iron
- Avoid dry cleaning clothes (alternatives to PERC include CO2 and silicone based techniques)

Reducing your Child's Toxic Load

- Avoid flame retardant materials in clothes (e.g.. pajamas; 100% cotton is preferable)
- Rinse off thoroughly and use Epsom salt bath after swimming in pools/hot tubs with chlorine
- For babies use glass bottles/BPA free alternatives
- Use natural, biodegradable personal care products and cleaning products for your home that are free of phthalates, parabens, triclosan, and BP-3 (<https://www.ewg.org/consumer-guides>)
- Avoid antibacterial soaps, mouthwash, toothpaste, etc.
- Fluoride free toothpaste
- Avoid Acetaminophen

Reducing your Child's Toxic Load

- Avoid contact with decayed or crumbling foam that may contain fire retardants; replace couches or old furniture with exposed foam
- Avoid putting stain treatments on new carpets or furniture
- Choose clothing that is not labeled stain or water repellent
- Avoid greasy fast foods (these wrappers are pretreated with PFCs)
- Consider having home tested for mold
- High quality supplements (www.labdoor.com)
- Think Dirty phone app – rates skincare, cosmetics, and personal care products



Before Detoxification

- Before detoxification, reduce toxic load (previous slides)
- Concentrate on GI health: daily bowel movements and address dysbiosis, probiotics
- Adequate Nutrition/multivitamin & multimineral
- Antioxidants:
 - Melatonin
 - Coenzyme Q10
 - Selenium, Zinc
 - Vitamin C
 - Carnitine
 - Vitamins A, D, E
 - Alpha lipoic acid
 - Curcumin

Before Detoxification

Support Methylation and Glutathione

- Folinic Acid
- MethylB12
- TMG/DMG
- Vitamin B6/Magnesium
- Vitamin B2
- TMG
- DMG
- BH4
- Glutathione precursors – NAC, glycine
- Reduced glutathione

Before Detoxification

Support Sulfation

- NAC
- Alpha Lipoic Acid
- Taurine
- Vitamin D
- Molybdenum, Biotin
- Epsom Salts baths (magnesium sulfate)

Before Detoxification

Address/Treat Mitochondrial Dysfunction

- L-Carnitine
- Coenzyme Q10
- Acetyl-L-Carnitine
- B vitamins
- Vitamin E/Vitamin C
- Alpha Lipoic Acid
- Methylcobalamin
- Folinic Acid
- Methylfolate
- Creatine
- NAC

Detoxification

Various options include:

- Pharmaceutical Chelation:
 - DMSA
 - EDTA
 - DMPS
- Herbals
- Sauna
- Homeopathy

Sweat!

Vitamin D Deficiency

Lower first trimester maternal serum levels of 25(OH) D (i.e.. Vitamin D) were associated with increased risk of developing autism in offspring.

Chen J., et al, [J Psychosom Res.](#) 2016 Oct;89:98-101

Mid-gestational Vitamin D deficiency was associated with an increased risk of ASD.

Vinkhuyzen, et al., [BJPsych Open.](#) 2017 Apr 10;3(2):85-90

Maternal vitamin D deficiency and the risk of autism spectrum disorders: population-based study.

- findings imply **gestational vitamin D substitution as a means of ASD prevention.**

Magnusson, et al, [BJPsych Open.](#) 2016 Apr 7;2(2):170-172

Omega 3 Fatty Acids

Maternal Dietary Fat Intake in Association With Autism Spectrum Disorders

- **Mothers in the lowest 5% of omega-3 fatty acid intake had a significant increase in offspring ASD risk**

Lyll, et al, [Am J Epidemiol.](#) 2013 Jul 15;178(2):209-20

Maternal Fatty Acid Status During Pregnancy and Child Autistic Traits: The Generation R Study

- **A lower maternal omega 3:omega 6 ratio ratio during pregnancy was associated with more autistic traits in the offspring**

Steenweg-de Graaff, et al., [Am J Epidemiol.](#) 2016 May 1;183(9):792-9

Folate Receptor Autoantibodies

- Folate receptor alpha autoantibodies have been associated with fetal abnormalities and cerebral folate deficiency-related developmental disorders.
- **Over 70% of the children with autism spectrum disorders (ASD) are positive for these autoantibodies and high-dose folinic acid is beneficial in treating these children.**

Desai, et al., [Mol Psychiatry](#). 2017 Sep;22(9):1291-1297

Folate Receptor Autoantibodies

- Study showed **antibodies to the rat FR α administered during gestation produce communication, learning and cognitive deficits** in a rat model that can be prevented by folinic acid and dexamethasone.
- In humans, **exposure to FR α autoantibodies during fetal development and infancy could contribute to brain dysfunction such as that seen in ASD** and other developmental disorders.
- **Identifying women positive for the autoantibody and treating them with high-dose folinic acid along with other interventions to lower the autoantibody titer are effective strategies that may be considered to reduce the risk of having a child with developmental deficits.**

Desai, et al., [Mol Psychiatry](#). 2017 Sep;22(9):1291-1297

Folate Receptor Autoantibodies

Folate receptor autoantibodies in women have been associated with.....cerebral folate deficiency syndrome and autism.

- **autoantibodies implicated in blocking folate transport to the fetus and to the brain in infants.**
- Authors report a woman with multiple pregnancy related complications diagnosed with autoantibodies to the folate receptor alpha.
- Treatment strategy with **folate supplementation and reducing the antibody titer proved effective in normal pregnancy outcome.**
- Treatment strategy described to prevent pregnancy related complications due to folate receptor autoantibodies.

[Shapira, Birth Defects Res A Clin Mol Teratol.](#) 2015 Dec;103(12):1028-30

Thyroid

Severe **maternal hypothyroxinemia** was associated with **almost 4-fold increase** in the odds of having a probable autistic child.

Román, et al., [Ann Neurol.](#) 2013 Nov;74(5):733-42

This study examined autism spectrum disorders (ASD) and thyroid stimulating hormone (TSH) levels measured in mid-pregnancy maternal serum and infant blood after birth. Adjusted logistic regression models showed **inverse associations between ASD and log transformed TSH levels** in maternal serum samples.

Yau, et al., [J Autism Dev Disord.](#) 2015 Mar;45(3):719-30

Thyroid peroxidase antibody (TPO-Ab) is an autoantibody involved in autoimmune thyroiditis. The **odds of autism were increased by nearly 80% among offspring of mothers who were TPO-Ab+ during pregnancy** compared to mothers negative for this autoantibody.

Brown, et al., [Prog Neuropsychopharmacol Biol Psychiatry,](#) 2015 Mar 3;57:86-92

Autism Risk Lowered by Taking Carnitine When Pregnant, Say Scientists

VYTAS A. BANKAITIS & ZHIGANG XIE, THE CONVERSATION 14 APR 2016

<https://www.sciencealert.com>

Inborn errors of metabolism (IEMs) occur with high incidence in human populations. Especially prevalent among these are inborn deficiencies in fatty acid β -oxidation (FAO), which are clinically associated with developmental neuropsychiatric disorders, including autism. We now report that neural stem cell (NSC)-autonomous insufficiencies in the activity of TMLHE (an **autism risk factor** that supports long-chain FAO by catalyzing **carnitine biosynthesis**), of CPT1A (an enzyme required for long-chain FAO transport into mitochondria), or of fatty acid mobilization from lipid droplets reduced NSC pools in the mouse embryonic neocortex. The collective data reveal a key role for FAO in controlling NSC-to-IPC transition in the mammalian embryonic brain and suggest NSC self renewal as a cellular mechanism underlying the association between IEMs and autism.

Xie, et al, [Cell Rep](#), 2016 Feb 9;14(5):991-999

Considerations Before and During pregnancy

- Start interventions at least 3 months before pregnancy
- Consider a summer conception
- Maintain a healthy weight
- Ensure adequate prenatal care
- Check thyroid and control thyroid function
- Avoid all medications, if possible
- Avoid stress, if possible
- Consider pregnancy spacing – space 2.5 years between pregnancies
- Avoid multiple ultrasounds
- Control gestational diabetes
- Avoid C-section and induction of labor, if possible
- Avoid delivery before 36 weeks, if possible

Slide Courtesy of Dan Rossignol, MD

Labs to Consider Before Pregnancy

- CBC, CMP
- TSH, free T3, free T4, thyroid
- Ferritin, Iron panel
- Magnesium
- Vitamin D
- Carnitine
- MTHFR, cerebral folate receptor autoantibodies
- CRP, Sed Rate, ANA

Slide Courtesy of Dan Rossignol, MD

Supplements to Consider Before and During Pregnancy

- Vitamin D3: 5000 IU per day
- Iron Supplementation
- Omega 3 fish oil (EPA + DHA): 3,000 mg per day
- Take an active form of folate (folinic acid or 5MTHF): 1600 mg per day (dad as well)
- Prenatal vitamin with 150 mcg/day of iodine and active forms of B12 (methylB12) and folate
- Carnitine – Acetyl-L-Carnitine 500 mg twice a day
- Choline 930 mg per day
- Calcium 1200-1400 mg per day

Slide Courtesy of Dan Rossignol, MD

Considerations After Delivery

- Breastfeed for at least 6 month; longer if possible; the longer the better
- Supplement infant with 1,000 IU of vitamin D3 for the first 3 years of life
- Add probiotics from birth at 10-20 billion units per day
- Avoid toxicants
- Eat an organic diet when possible
- Filter the air and water
- Avoid acetaminophen use

Slide Courtesy of Dan Rossignol, MD