



Fertility and Environmental Toxins

Dr. Joseph Pizzorno, ND

President Emeritus, Bastyr University

Editor, *Integrative Medicine: A Clinician's Journal*

Chair, Board of Directors, Institute for Functional Medicine

Chair, Scientific Advisory Board, Bioclinic Naturals

President, SaluGenecists, Inc.

mail2@DrPizzorno.com

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Houston, We Have a Problem!

Erin Brockovich

- If current decline in sperm count continues at current rate, men will be sterile by 2045



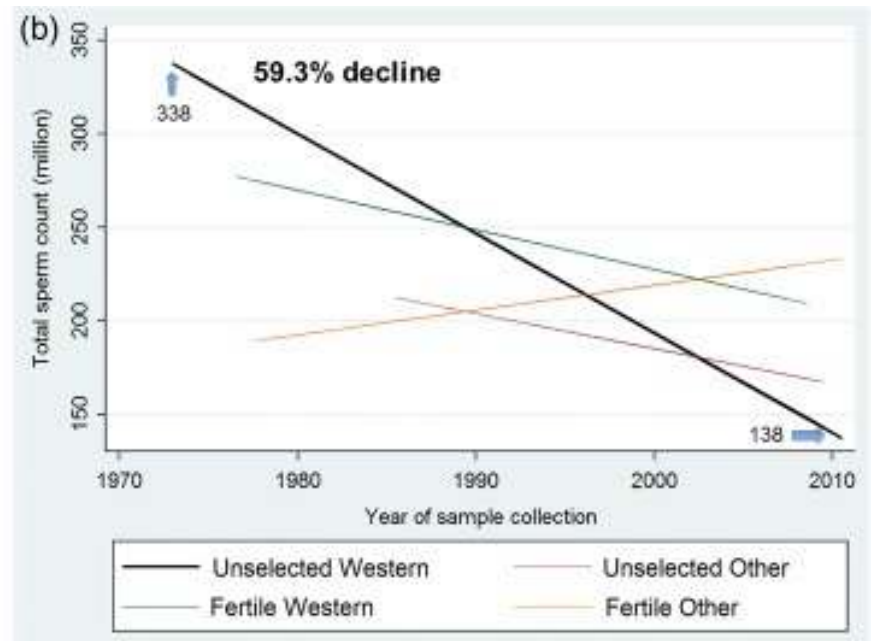
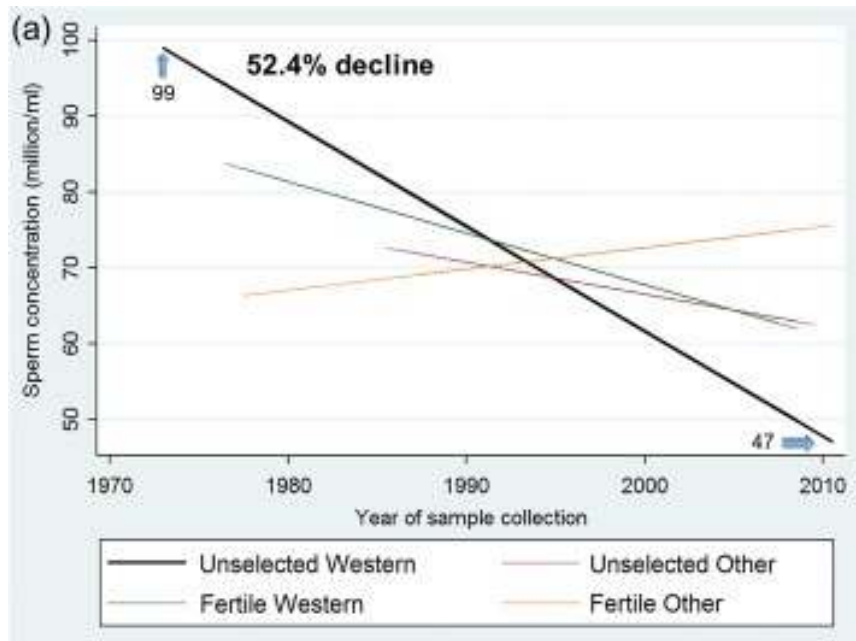
Overview

- Worldwide Infertility Epidemic
- How Toxins Cause Infertility
- Specific Toxins and Infertility
- Portion of Infertility Due to Toxins
- Clinical Takeaways



We Truly Have A Serious Problem

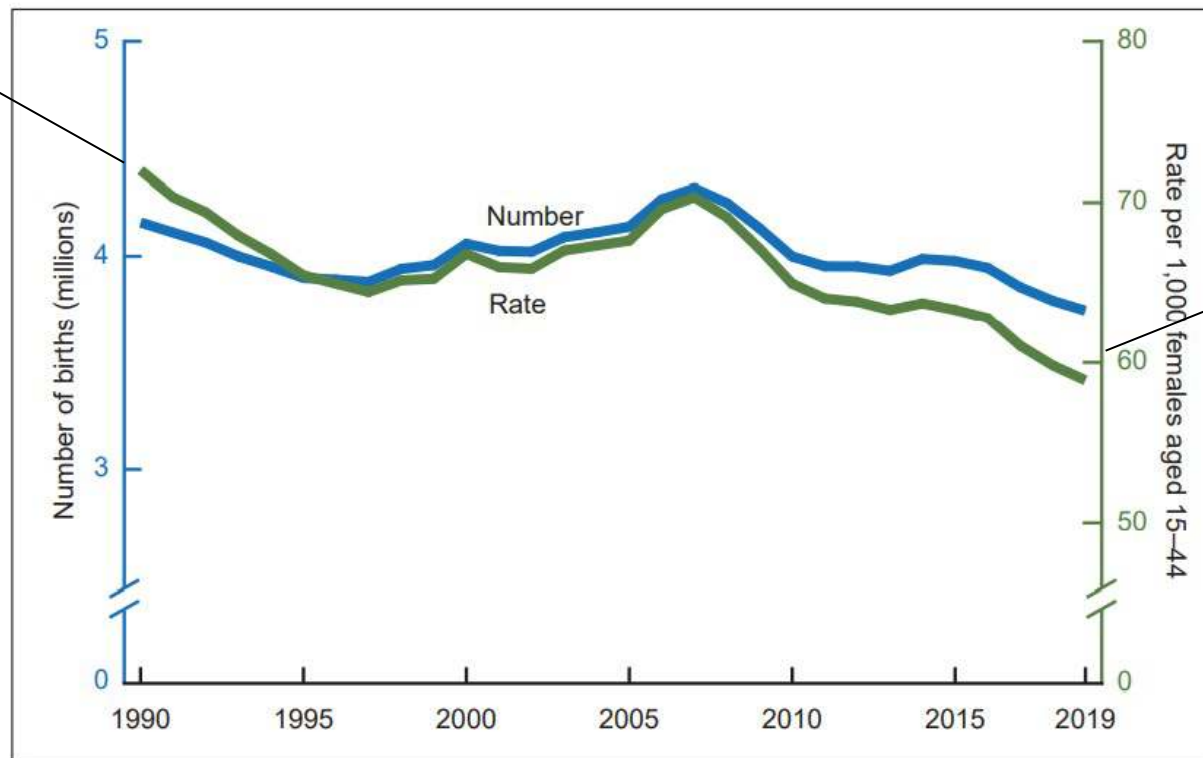
Sperm counts dropped 50-60% since 1973 to 2011





Fertility Rate in US Decreasing Relentlessly

Figure 2. Number of live births and general fertility rates: United States, final 1990–2018 and provisional 2019



SOURCE: NCHS, National Vital Statistics System, Natality.



Infertility in Canada

- Growing prevalence:
 - Currently 16%
 - Doubled since 1980
- Causes:
 - 3 times out of 10, the cause is in men.
 - 4 times out of 10, the cause is in women.
 - 2 times out of 10, the cause is a mix of factors from both male and female.
 - 1 time out of 10, at first, no specific cause can



Canadian Government Explanation

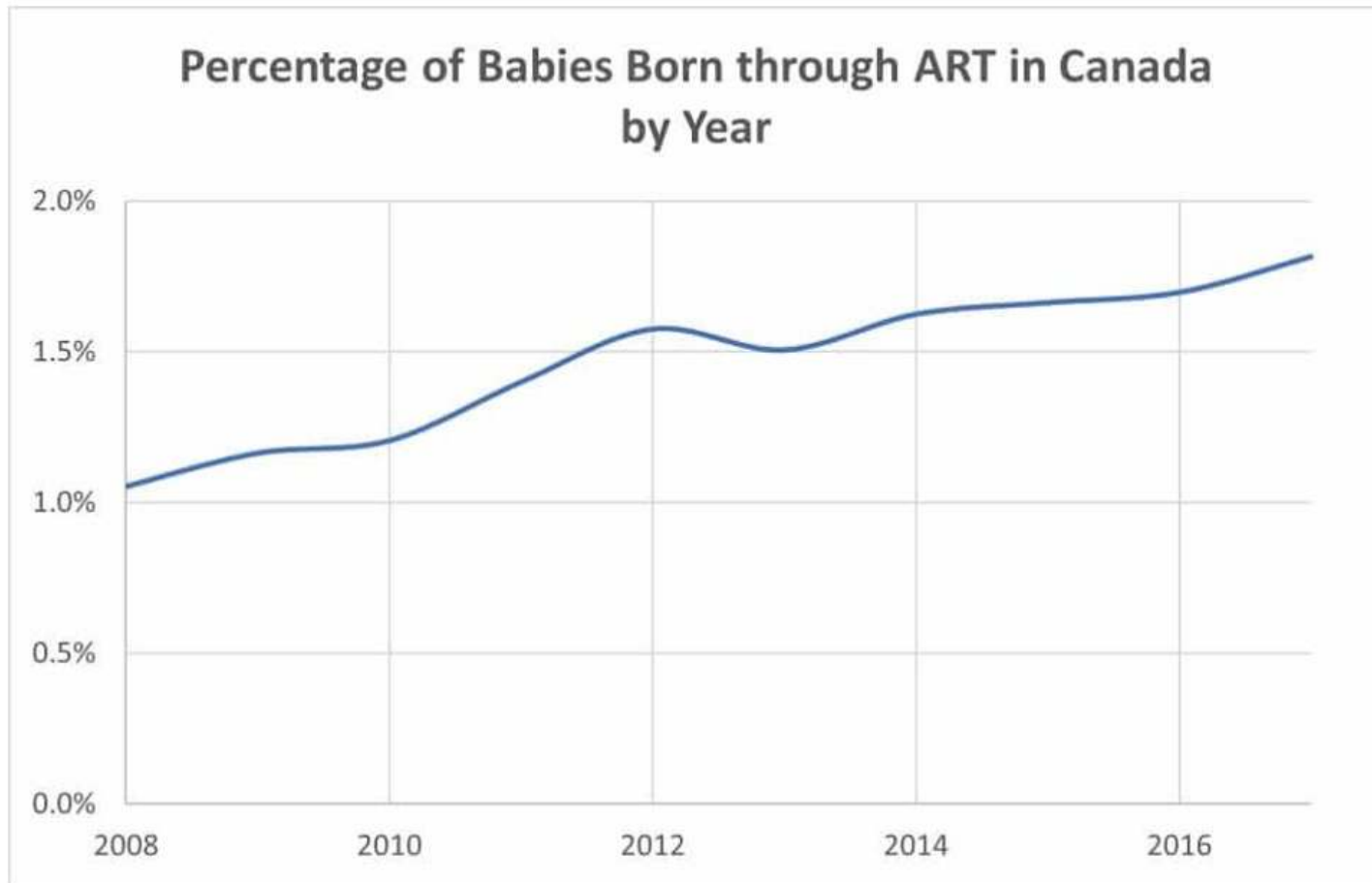
Causes of infertility **in women** may include:

- age (fertility decreases after age 35)
- problems producing eggs (which shows up when she has no period/menstrual cycle, or no regular one)
- having a sexually transmitted infection (STI), like Chlamydia (which can cause blockages in the fallopian tubes)
- problems in the uterus (like fibroids or polyps)
- problems with the fallopian tubes (like missing tubes or blockages)
- endometriosis (excess of tissue that gathers around the reproductive organs)
- hormonal imbalances
- early menopause (before age 40)

**How about rampant
Nutrient Deficiencies
Environmental Toxins
??**



Growing Percentage of Canadian Children Born Through ART



Source of US Population Toxicant Load



2019

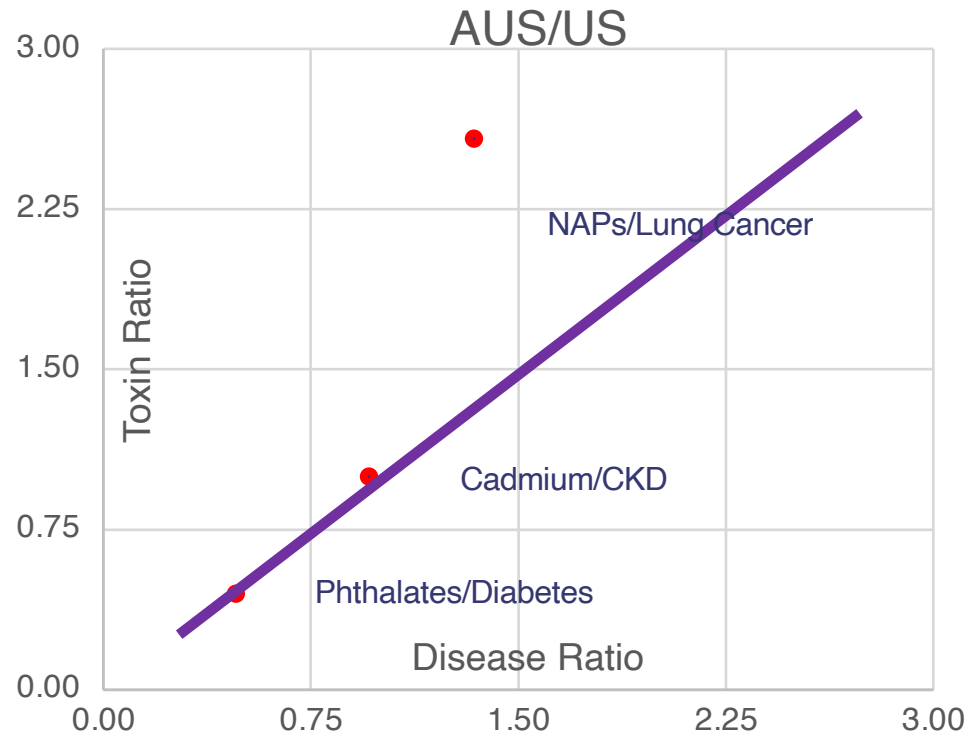
Fourth National Report on Human Exposure to Environmental Chemicals
Updated Tables, January 2019, Volume One



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

Toxin/Disease Ratios Remarkably Similar

Limited data
Not publishable
Illustrative Only





Canadian Toxin Levels

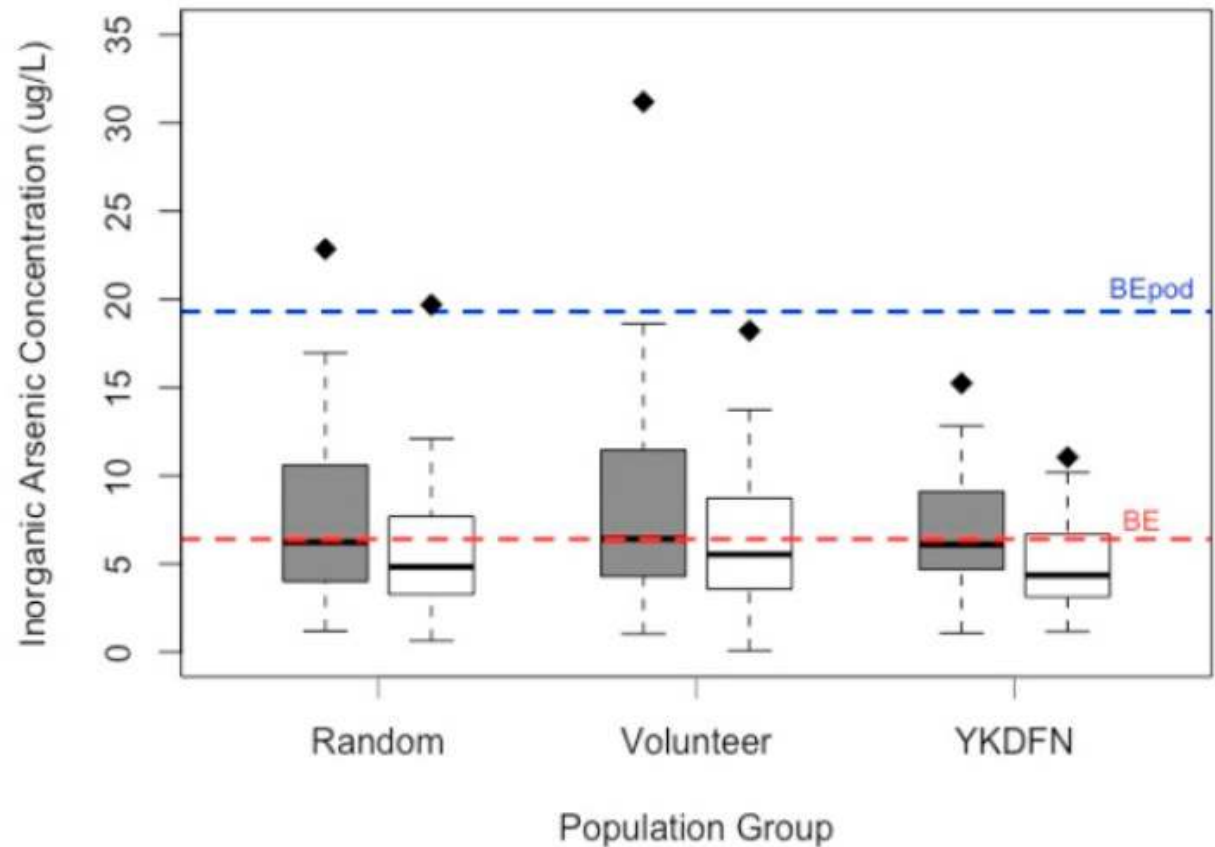
Toxin	US	Canada	PMID/Year	Notes
Arsenic ug/L	6.8	7.2	22164561 (2011)	
BPA ug/g cr	1.5	1.2	20973429 (2010)	
Cadmium ug/g cr	0.18	0.46	26885840 (2016)	
Lead ug/L	2.2	1.4	20973429 (2010)	
Phthalates ug/L	9.0	12	23419587 (2013)	MBzP

Reference PMIDs are for Canadian numbers



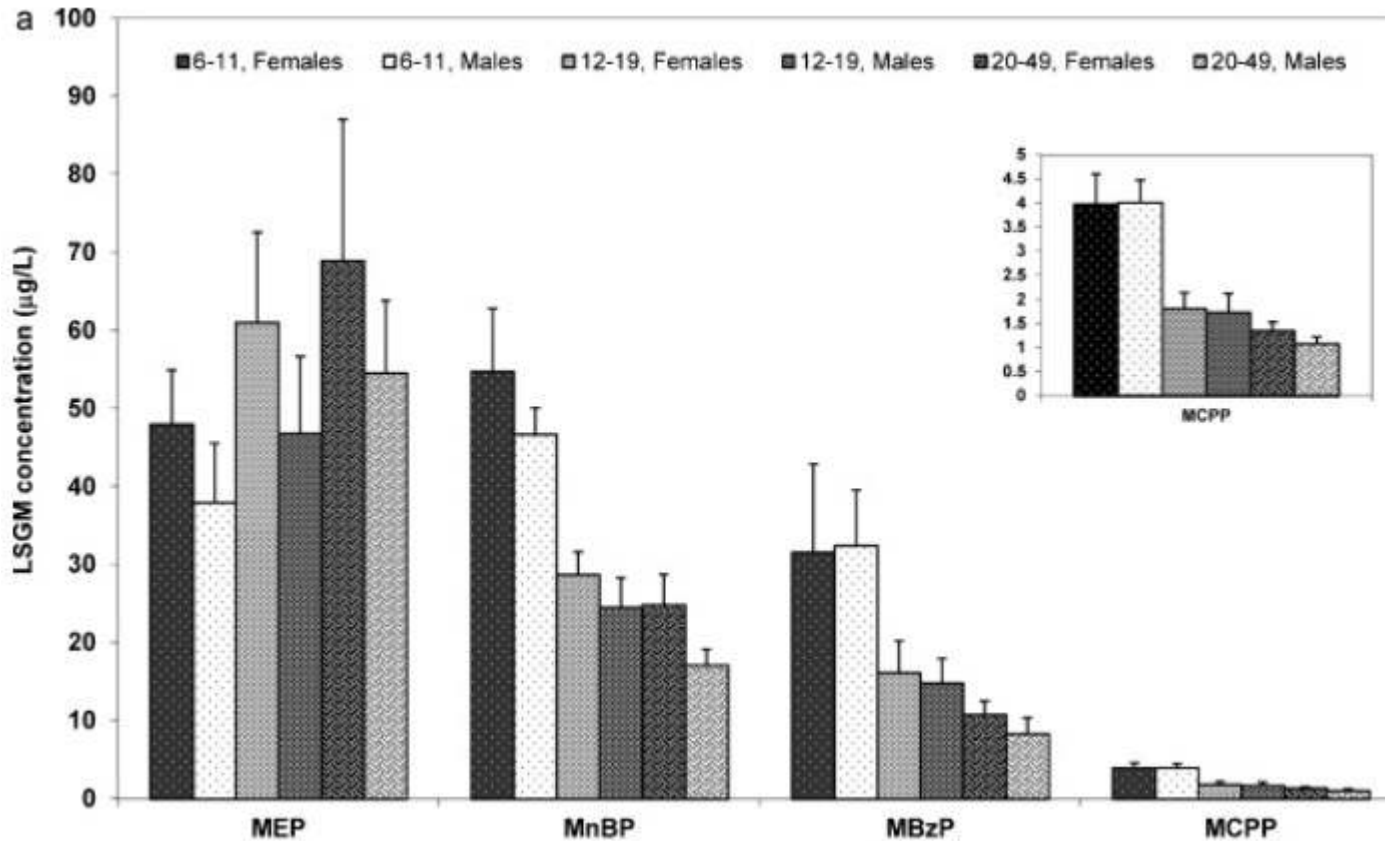
Arsenic Levels in Canada

- NW Territories





Phthalates Canada



Saravanabhavan G, Guay M, Langlois É, Giroux S, Murray J, Haines D. Biomonitoring of phthalate metabolites in the Canadian population through the Canadian Health Measures Survey (2007-2009). *Int J Hyg Environ Health*. 2013;216(6):652-661



How Toxins Impair Female Fertility

- **PCOS**
 - PCBs
 - Phthalates
 - Arsenic
- **Reduction in luteal phase LH**
 - Solvent exposure (usually occupational, esp. acetone)
- **Miscarriage/Fetal abnormalities**
 - PCBs
 - Pentachlorophenol (PCP)
 - Agent Orange exposure
 - Smoking
 - PAHs



How Toxins Impair Male Fertility

- **Low testosterone**
 - Phthalates
 - PFOS
 - PBDE
- **Decrease in sperm number & function**
 - Pesticides
 - Metals
 - Air pollutants
 - Phthalates
 - PCB 138
- **Erectile dysfunction**
 - Solvents
 - Pesticides
 - Metals



How Toxins Impair Fetal Development

- **Fetal death/Spontaneous abortion**
 - Arsenic
 - Organophosphates
- **Low birth weight/head size**
 - Triazine herbicides
 - Air pollutants (CO, NO₂, O₃, PM 2.5)
- **Increased fetal abnormalities**
 - BPA
 - Cadmium



How Toxins Decrease IVF Success

- **Decreased # oocytes retrieved**
 - BPA
- **Failed implantation**
 - PCBs
- **Failed fertilization**
 - Organochlorine pesticides
 - Parabens
 - PBDEs



The Toxins Causing Infertility Metals and Metalloids



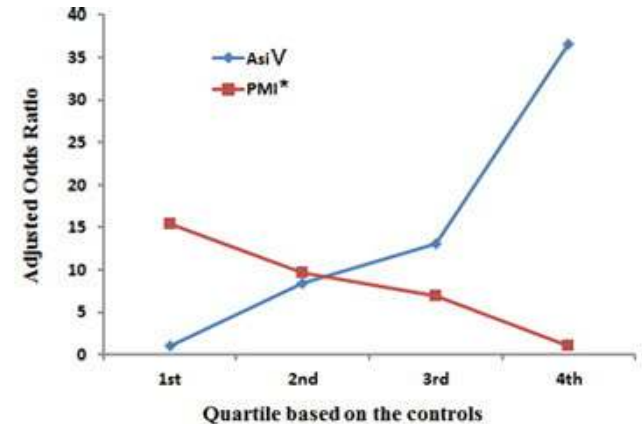
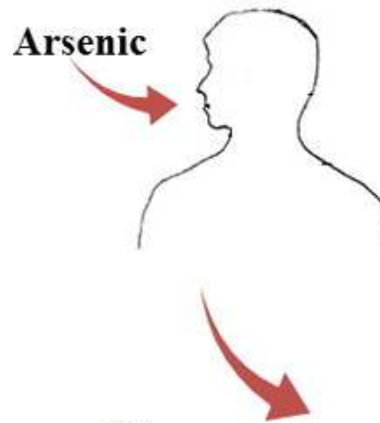
Arsenic

- Especially damaging to males
- Impairs many aspects of spermatogenesis
- Strong correlation with prostate cancer



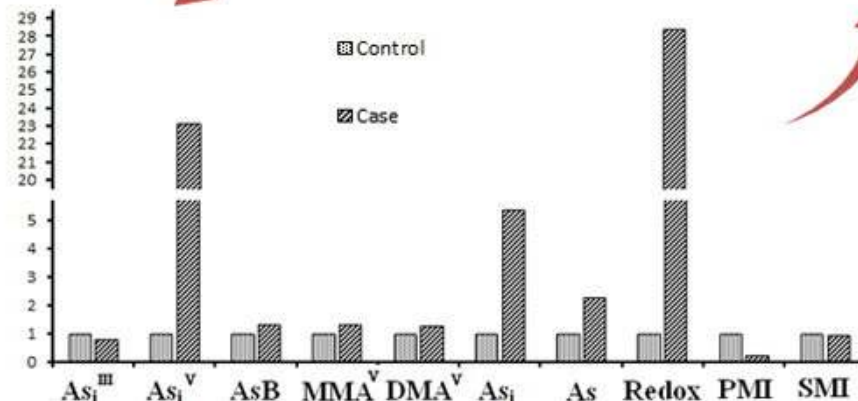
Arsenic Devastating to Male Fertility

- Males with “Unexplained male infertility”
- Highest quartile: OR = 36.5!



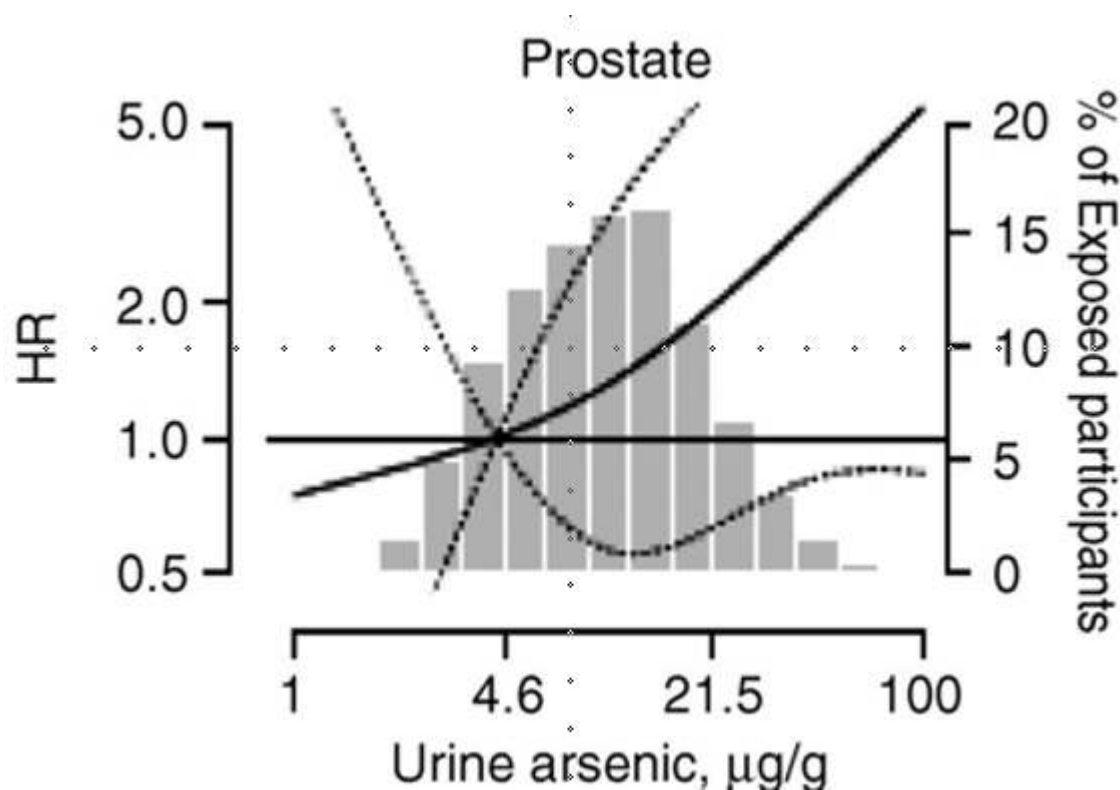
Dose-dependent association of arsenic with adjusted odds ratio (AOR) of unexplained male infertility.

*The values of PMI decreased from the first to fourth quartile.





Arsenic Big Factor in Prostate Cancer



García-Esquinas E, Pollán M, Umans JG, et al. Arsenic exposure and cancer mortality in a US-based prospective cohort: the strong heart study. *Cancer Epidemiol Biomarkers Prev.* 2013 Nov;22(11):1944-53

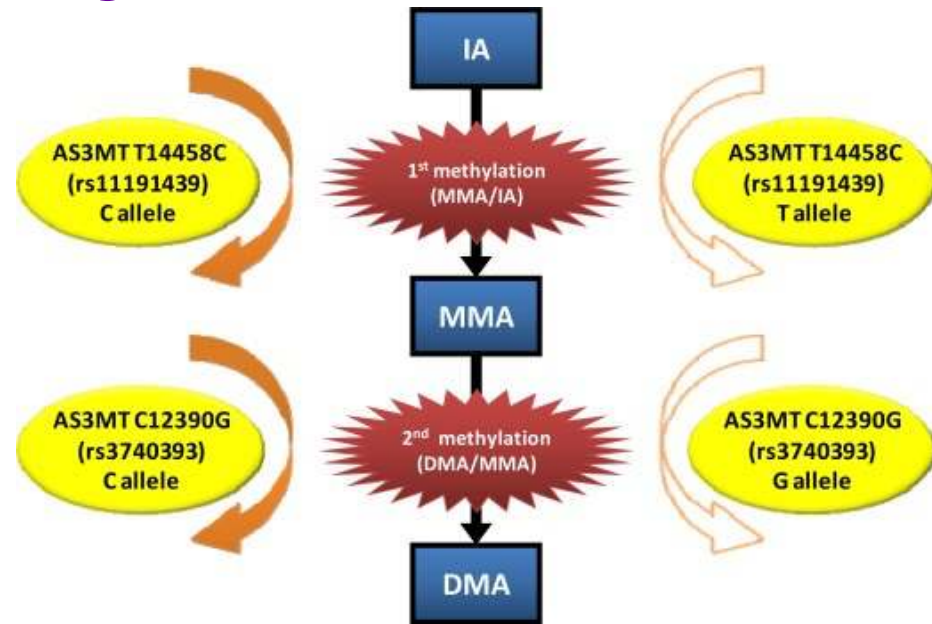


Assessment - Direct

- Random or first morning urine
 - <6 ug As/g creatinine has little disease significance
 - >12 ug As/g creatinine indicate higher risk for cardiovascular disease, diabetes, respiratory problems, cancers and neurological dysfunction
 - >30 ug/g creatinine typically means MMA levels high enough to cause genotoxicity
- **THRESHOLDS IMPACTED BY SNPs!**

Genetics Hugely Important

- C allele of AS3MT 14458 (rs11191439) higher 1st methylation capacity than T
- C allele of AS3MT 12390 (rs3740393) higher 2nd methylation capacity than G
- Fast 1st methylation
+
Slow 2nd methylation
=
Greatly increased As toxicity
- 1% of population



rs11191439 prevalence

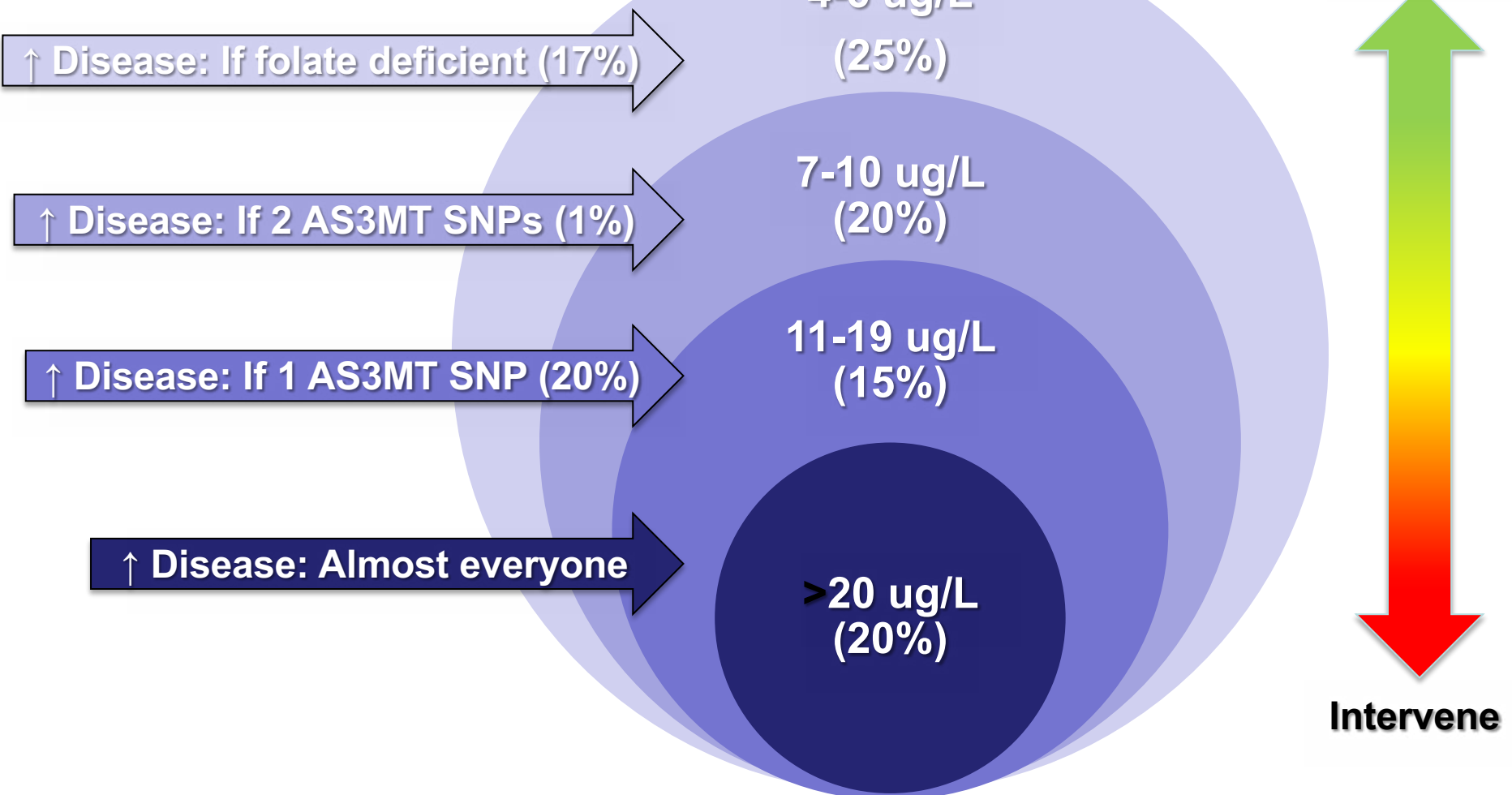
CC: 0.013

CT: 0.181

TT: 0.805



Arsenic in Water

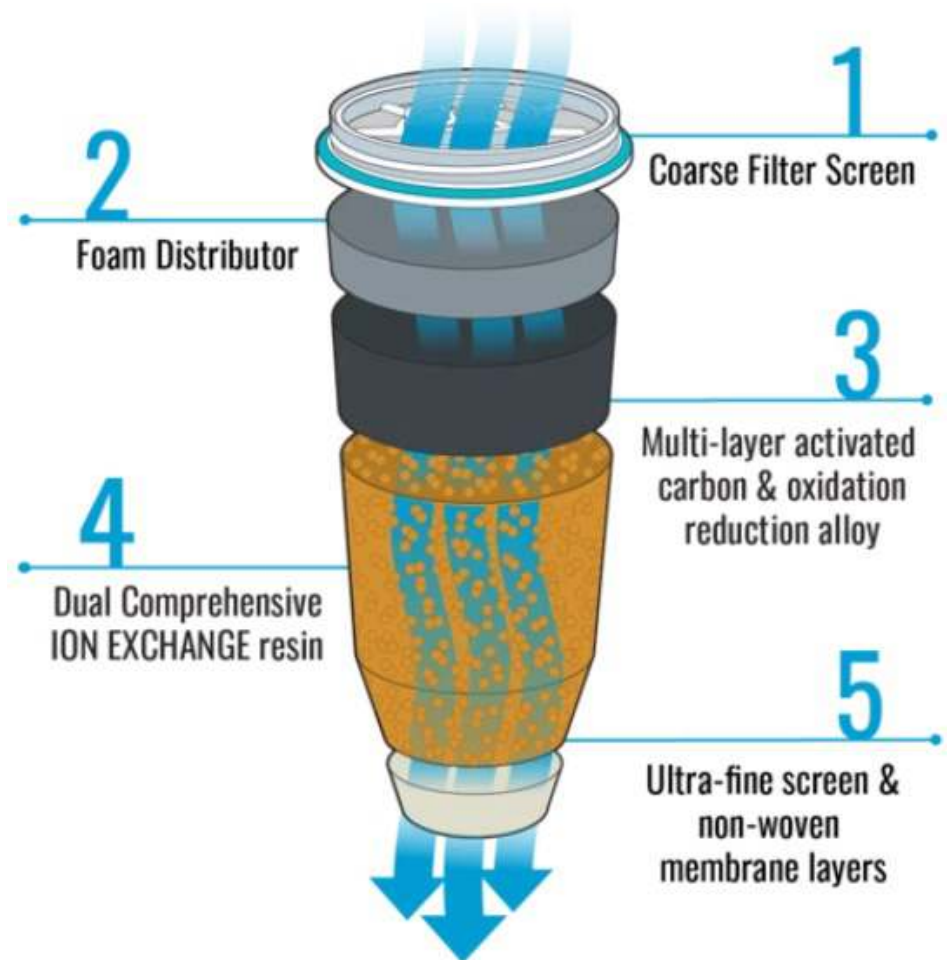


Prevalence from research; thresholds only estimated at this time; water estimated from urine)



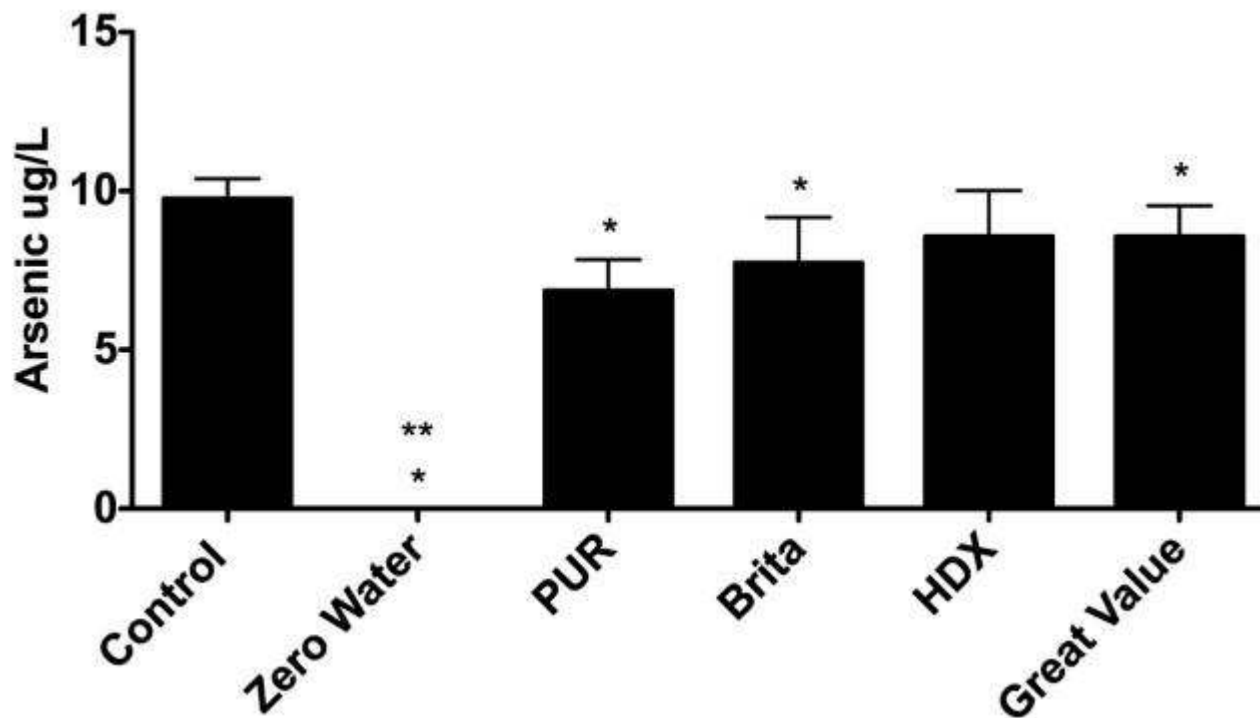
Zero Water Technology

- No commercial relationship.
- Tried personally and was impressed.
- Key technologies:
 - Activated carbon.
 - Oxidation alloy.
 - Ion exchange.





Tabletop Filtration



Barnaby R, Liefeld A, Jackson BP, Hampton TH, Stanton BA. Effectiveness of table top water pitcher filters to remove arsenic from drinking water. Environ Res. 2017 Oct;158:610-615. PMID: 28719869



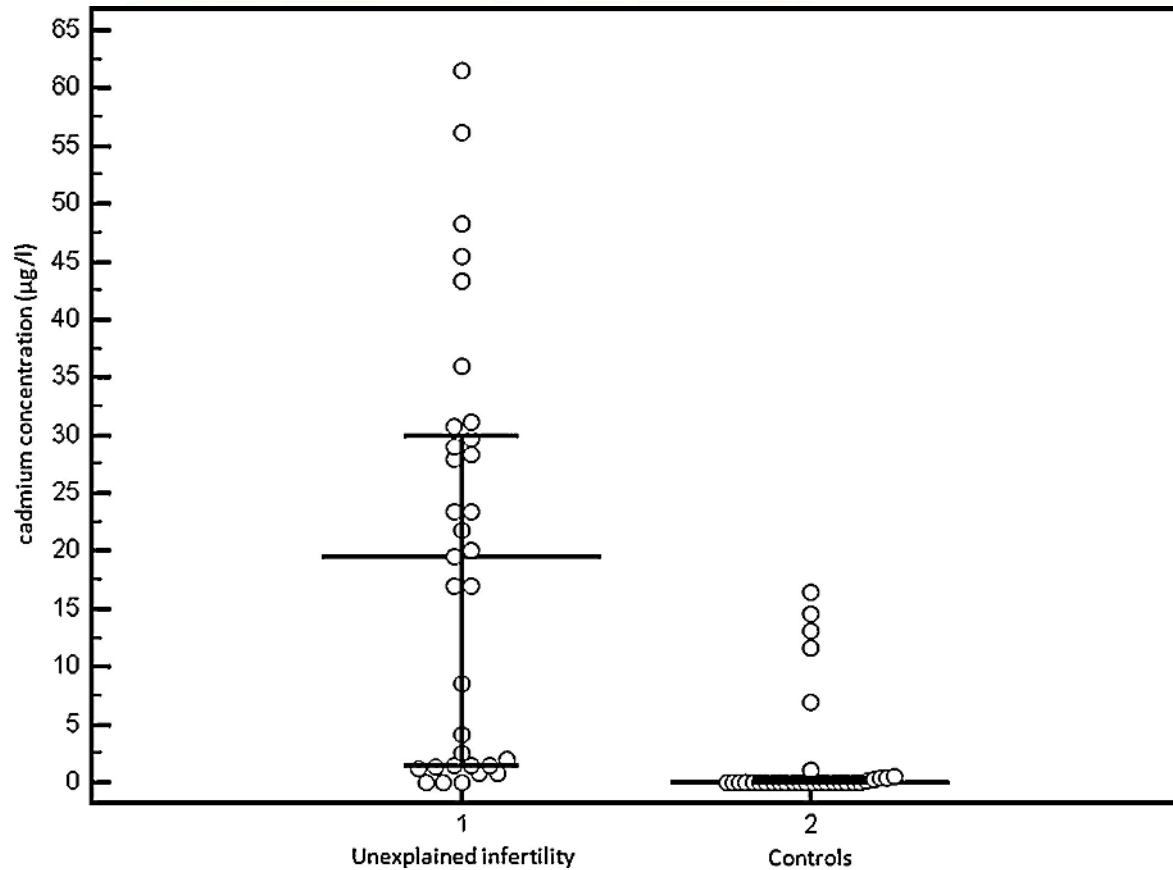
Cadmium

- Directly toxic to ovaries



Cadmium Damages Female Fertility

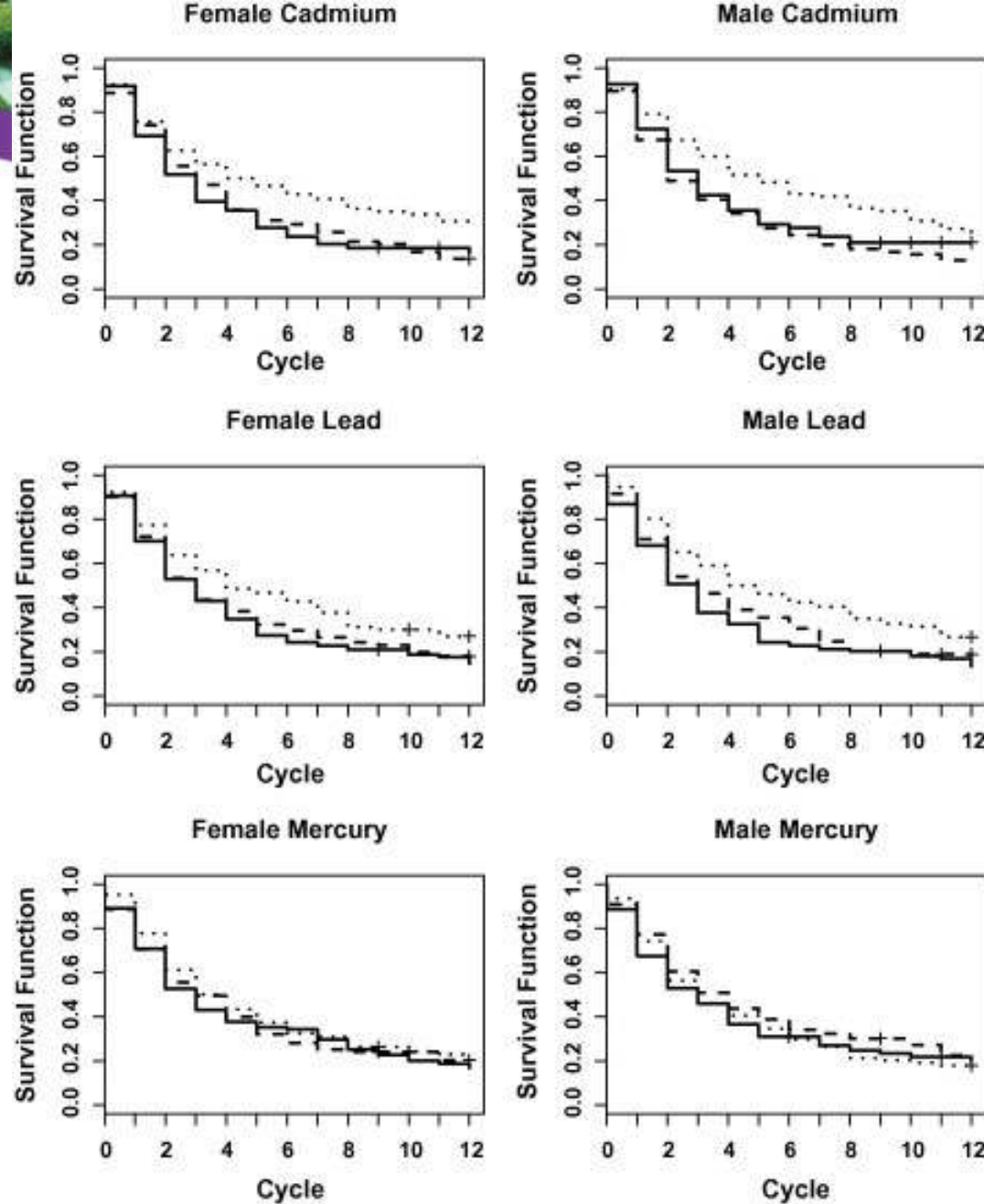
- Cadmium in endometrial tissue
- OR = 18.9!





Cadmium and Lead Decrease Fertility in Top Tertial Body Load

- Time to pregnancy
- Dotted line highest heavy metal level





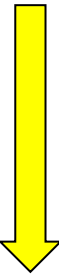
Cadmium

Urinary Cadmium (creatinine corrected) (1999 – 2010)

CAS Number 81271-94-5

Geometric mean and selected percentiles of urine concentrations (in $\mu\text{g/g}$ of creatinine) for the U.S. population from the National Health and Nutrition Examination Survey.

Categories (Survey Years)	Geometric Mean (95% conf. interval)	50th Percentile (95% conf. interval)	75th Percentile (95% conf. interval)	90th Percentile (95% conf. interval)	95th Percentile (95% conf. interval)	Sample Size
Total population (1999 - 2000**)	.181 (.157-.209)	.219 (.199-.238)	.423 (.391-.446)	.712 (.645-.757)	.941 (.826-1.07)	2257
Total population (2001 - 2002**)	.199 (.181-.218)	.212 (.194-.232)	.404 (.377-.440)	.690 (.630-.754)	.919 (.813-.998)	2689
Total population (2003 - 2004)	.210 (.201-.219)	.208 (.189-.226)	.412 (.381-.438)	.678 (.650-.716)	.940 (.833-1.04)	2543
Total population (2005 - 2006)	.189 (.169-.210)	.180 (.160-.200)	.370 (.310-.430)	.650 (.590-.720)	.910 (.770-1.08)	2576
Total population (2007 - 2008)	.193 (.177-.210)	.190 (.180-.210)	.370 (.330-.410)	.660 (.580-.740)	.960 (.840-1.06)	2627
Total population (2009 - 2010)	.191 (.184-.199)	.180 (.170-.190)	.370 (.340-.400)	.680 (.630-.730)	.910 (.840-1.00)	2848



- Primary sources: cigarette smoking, soy (chemically-grown)
 - Threshold: 0.40 $\mu\text{g/g}$ (no safe levels)
- ⇒ >20% of population

Fourth National Report on Human Exposure to Environmental Chemicals. Updated Tables, January 2019, Volume One

García-Esquinas E, Pollan M, Tellez-Plaza M, et al. Cadmium exposure and cancer mortality in a prospective cohort: the strong heart study. Environ Health Perspect. 2014;122(4):363-70



Assessment

- Highly controversial since poor correlation between blood, urine and tissue levels
- Urinary Cd
 - Threshold: 0.40 ug/g (no safe levels)
- Doctors Data
 - <https://www.doctorsdata.com>



Intervention

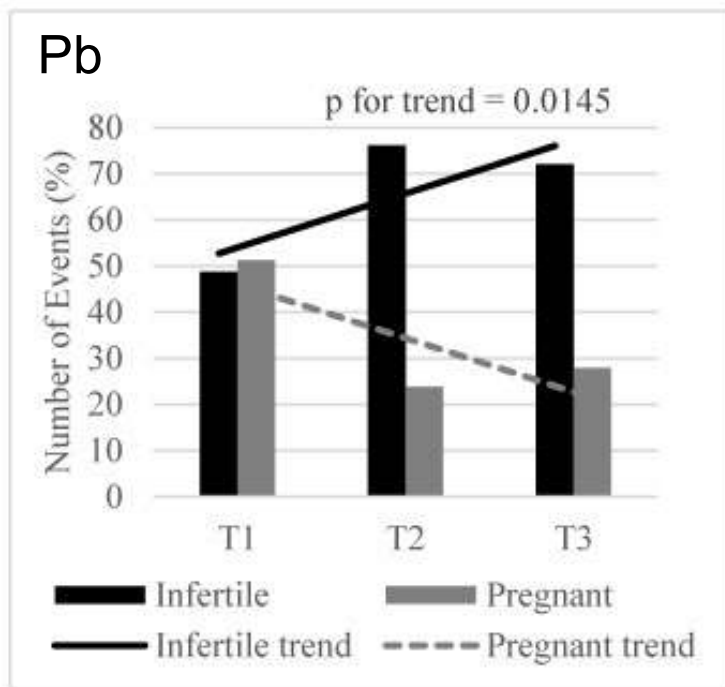
- Key avoidance strategies:
 - No smoking
 - Do not eat foods grown with high-phosphate “fertilizers” especially soybeans
- **Sauna**
- Antioxidants
- Trace minerals



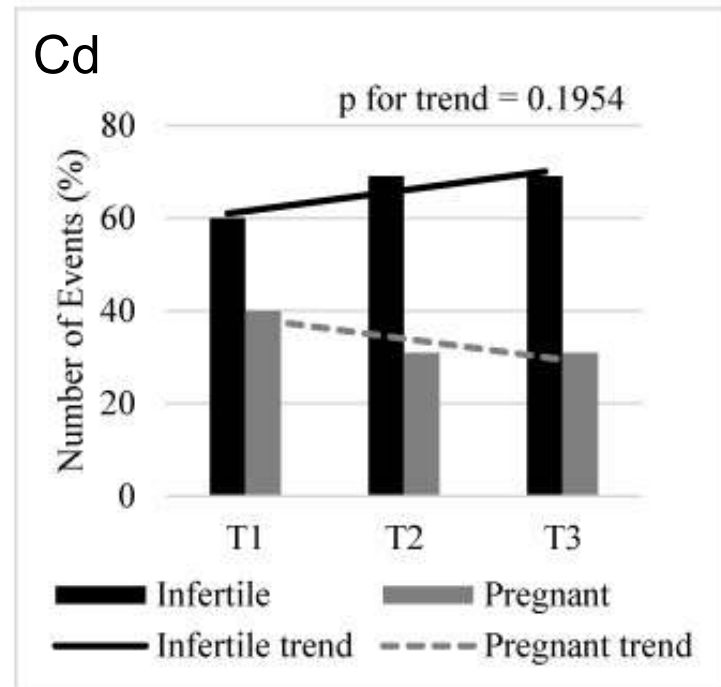
Lead



Lead Decreases Female Fertility



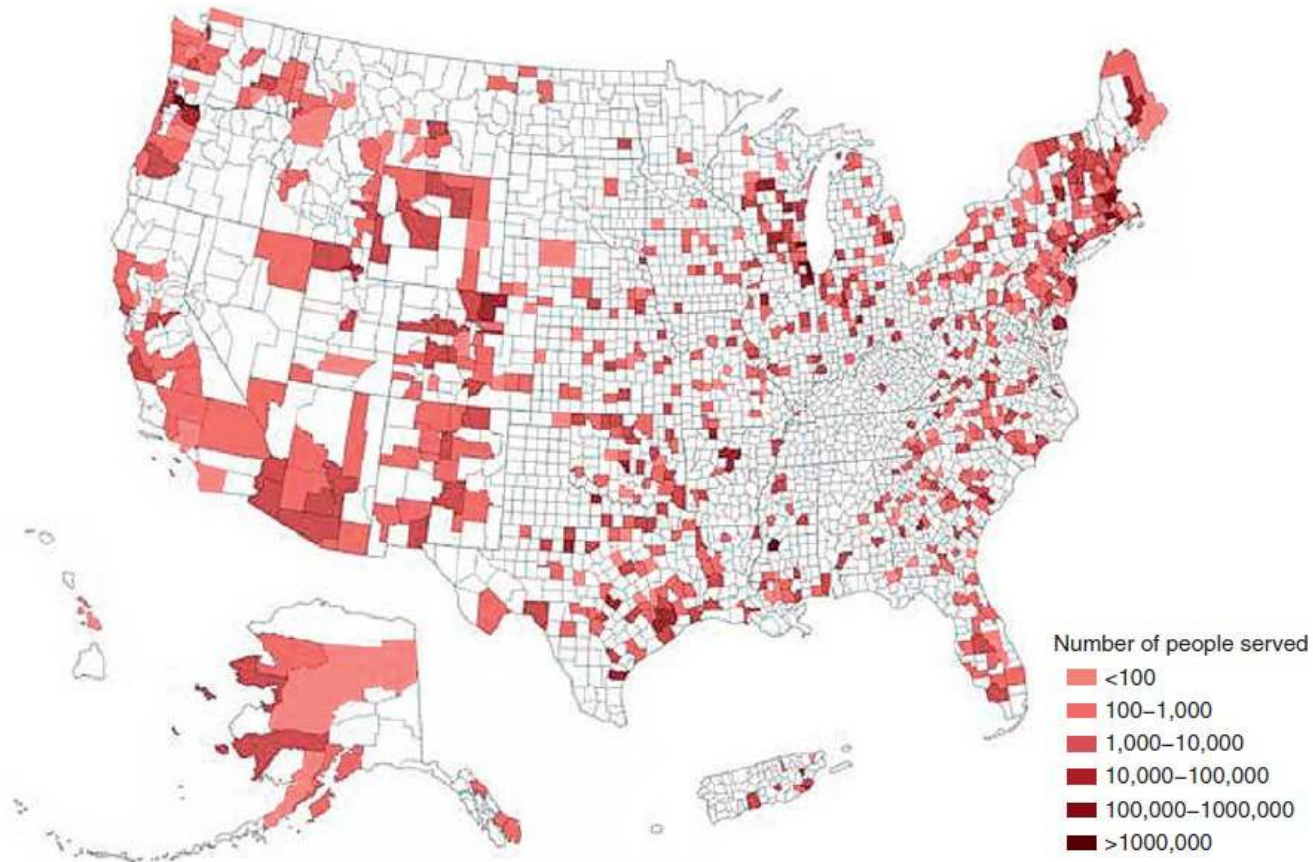
(a)



(b)



People Served by Water Systems with Lead > 15 PPB





Lead Assessment

- Blood lead
 - Children threshold: 3 ug/dL (NO safe levels)
 - Adult threshold: 5.0 ug/dL (NO safe levels)
- Readily available from standard laboratories



Lead Intervention

- Maintain bone
- If home built or water supply to the house installed before 1987, test water in home
- Supplements:
 - Calcium: 500 bid
 - Vitamin C: 500 bid
 - NAC: 500 mg bid
- If high blood lead
 - EDTA: oral, IV (physician protocol)
 - DMSA: oral, 250 mg/3d

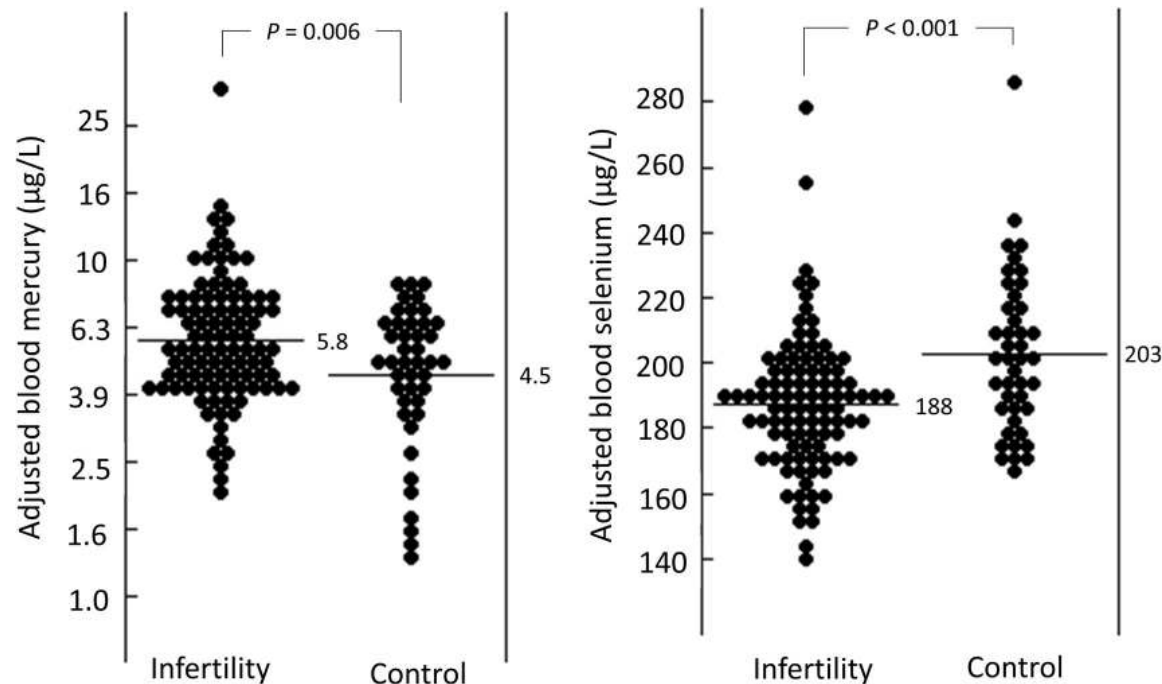


Mercury



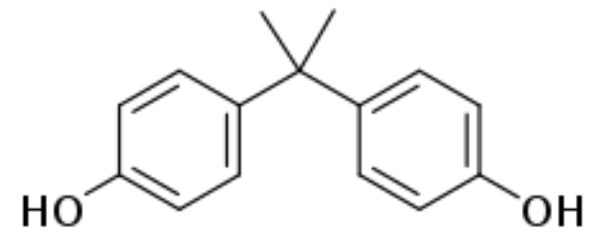
Mercury Damages Female Fertility

- Selenium protects against mercury
- Se/Hg ratio highly predictive of infertility





The Toxins Causing Infertility Chemicals



Bisphenols (BPx)



Canadian Government BPA Position

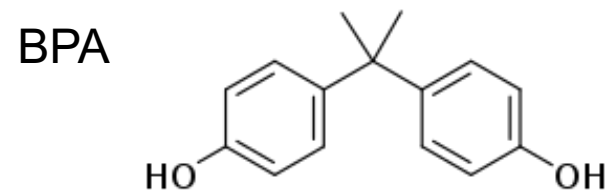
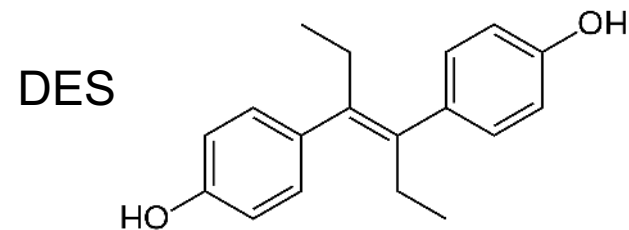
Health Canada's Food Directorate has concluded that the current dietary exposure to BPA through food packaging uses is not expected to pose a health risk to the general population, including newborns and infants.

However, due to the uncertainty raised in some animal studies relating to the potential effects of low levels of BPA, the Government of Canada is taking action to enhance the protection of infants and young children. It is therefore recommended that the general principle of ALARA ¹ (as low as reasonably achievable) be applied to continue efforts on limiting BPA exposure from food packaging applications to infants and newborns, specifically from pre-packaged infant formula products as a sole source food, for this sensitive segment of the population.



BPA — Troubled History

- BPA and DES are synthetic oestrogens developed during the 1930s:
 - DES ‘won’ and was prescribed for pregnant women.
 - Discontinued due to urogenital cancers in children and many other clinical problems.
 - Very similar chemical structures.
- BPA ‘put on the shelf’ until 1950s when its ability to harden plastics was discovered.
- So widely used very difficult to avoid exposure:
 - Technically non-persistent, but practically semi-persistent.





Bisphenols

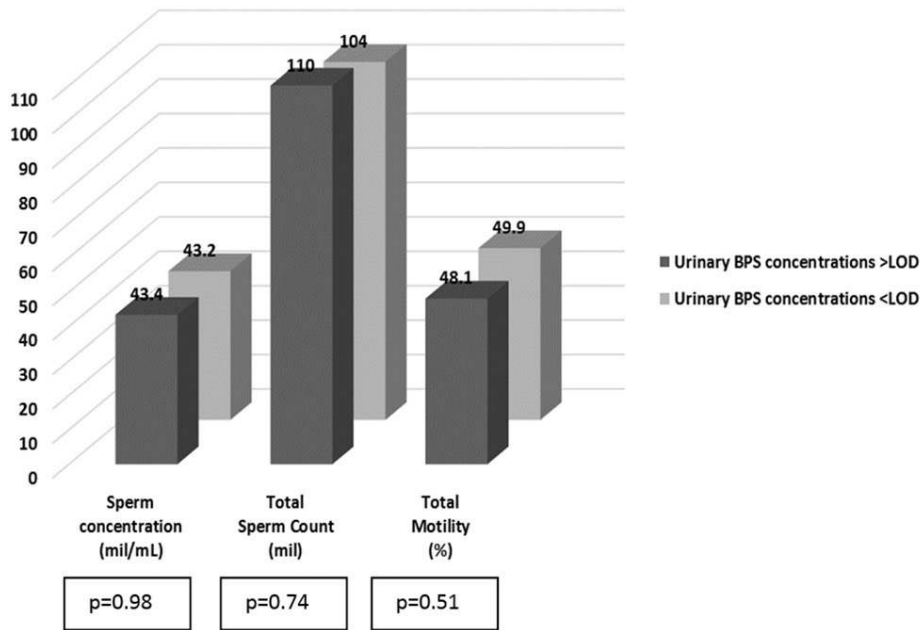
- BPA inconsistent correlation with infertility
- BPS strong correlation with infertility in overweight men
- As average BPA levels go down, other bisphenols go up



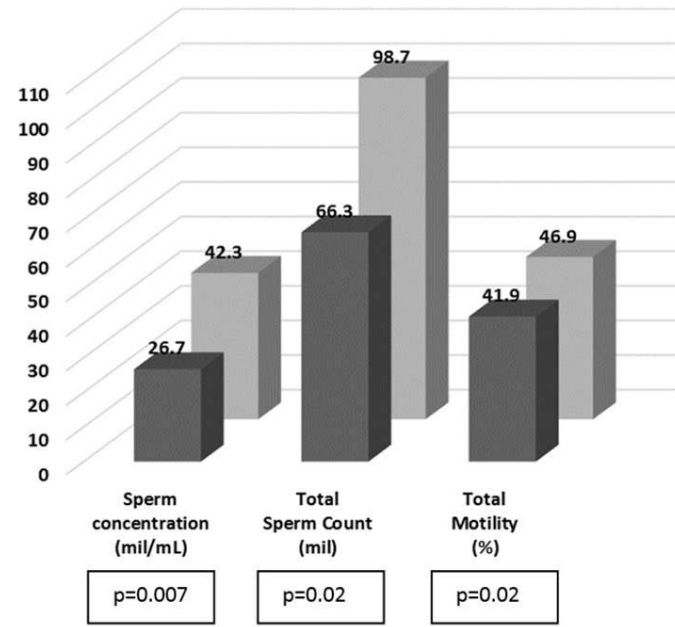
Bisphenols Decreases Male Fertility

- Damaging effects primarily in overweight men

52 men (113 semen samples) with BMI <25 kg/m²



106 men (225 semen samples) with BMI ≥ 25 kg/m²



Ghayda RA, Williams PL, Chavarro JE, et al. Urinary bisphenol S concentrations: Potential predictors of and associations with semen quality parameters among men attending a fertility center. Environ Int. 2019 Oct;131:105050

BPA Levels Correlate with Obesity

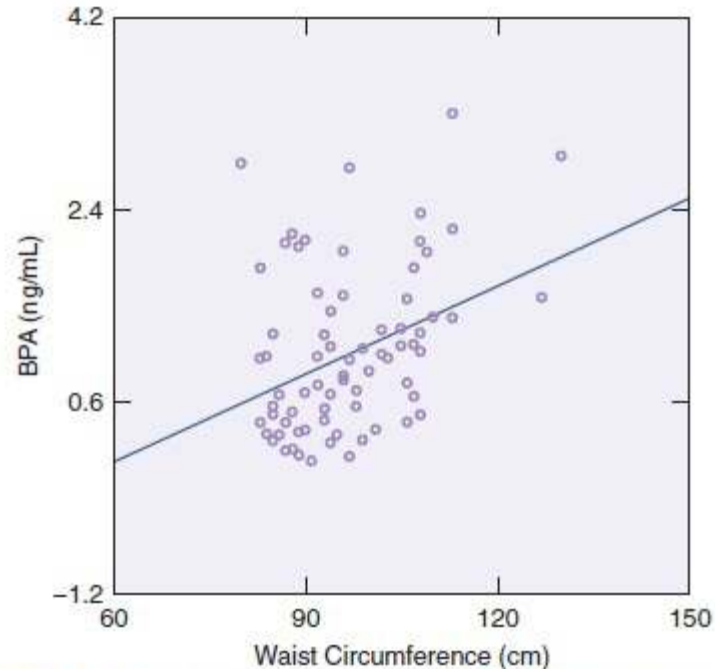


FIG. 25.3 BPA correlates with visceral fat. (From Savastano, S., Tarantino, G., D'Esposito, V., Passaretti, F., Cabaro, S., Liotti, A., Liguoro, D., Perruolo, G., Ariemma, F., Finelli, C., Beguinot, F., Formisano, P., Valentino, R. [2015]. Bisphenol-A plasma levels are related to inflammatory markers, visceral obesity and insulin-resistance: A cross-sectional study on adult male population. *Journal of Translational Medicine*, 13,169.) Licensed under a Creative Commons Attribution-ShareAlike 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>).



BPA Replaced w Other Bisphenols

Urinary Bisphenol A (creatinine corrected) (2003 – 2010)

CAS Number 80-05-7

Geometric mean and selected percentiles of urine concentrations (in $\mu\text{g/g}$ of creatinine) for the U.S. population from the National Health and Nutrition Examination Survey.

Categories (Survey Years)	Geometric Mean (95% conf. interval)	50th Percentile (95% conf. interval)	75th Percentile (95% conf. interval)	90th Percentile (95% conf. interval)	95th Percentile (95% conf. interval)	Sample Size
Total population (2011 - 2012)	2003/4 = 2.58 1.28 (1.20-1.36)	1.30 (1.20-1.40)	3.00 (2.70-3.30)	5.60 (4.90-6.50)	9.40 (7.70-11.2)	2489
Total population (2013 - 2014)	2013/4 = 1.28 1.28 (1.20-1.36)	1.20 (1.20-1.40)	2.50 (2.40-2.70)	4.90 (4.10-5.60)	7.70 (6.80-8.30)	2686

Urinary Bisphenol F (creatinine corrected) (2013 – 2014)

CAS Number 80-05-7

Geometric mean and selected percentiles of urine concentrations (in $\mu\text{g/g}$ of creatinine) for the U.S. population from the National Health and Nutrition Examination Survey.

Categories (Survey Years)	Geometric Mean (95% conf. interval)	50th Percentile (95% conf. interval)	75th Percentile (95% conf. interval)	90th Percentile (95% conf. interval)	95th Percentile (95% conf. interval)	Sample Size
Total population (2013 - 2014)	2013/4 = 0.53 0.53 (.47-.60)	0.44 (.385-.515)	1.07 (.899-1.21)	3.33 (2.39-4.76)	8.39 (5.90-12.0)	2680

Urinary Bisphenol S (creatinine corrected) (2013 – 2014)

CAS Number 80-05-7

Geometric mean and selected percentiles of urine concentrations (in $\mu\text{g/g}$ of creatinine) for the U.S. population from the National Health and Nutrition Examination Survey.

Categories (Survey Years)	Geometric Mean (95% conf. interval)	50th Percentile (95% conf. interval)	75th Percentile (95% conf. interval)	90th Percentile (95% conf. interval)	95th Percentile (95% conf. interval)	Sample Size
Total population (2013 - 2014)	2013/4 = 0.43 0.43 (.37-.47)	0.35 (.352-.411)	.797 (.690-.903)	1.80 (1.49-2.10)	3.33 (2.60-4.68)	2680



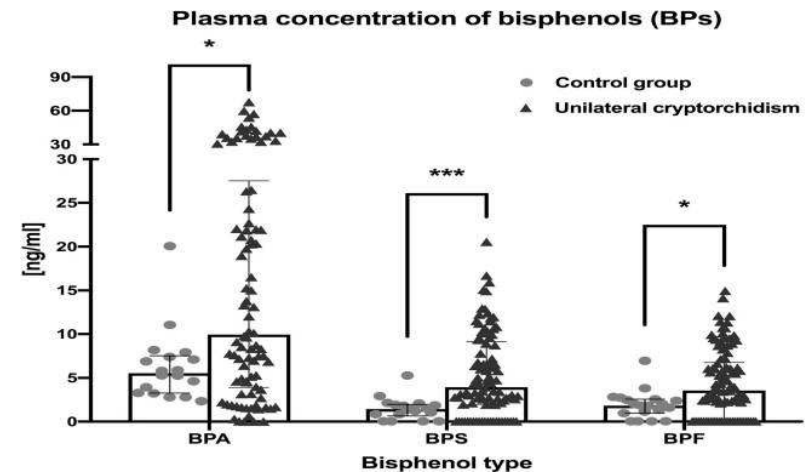
Alternatives Are NOT Safer!

- Typical substitutes are BPF, BPS, BPZ
- Very similar endocrine disruption
- Considered semi-persistent because so prevalent in society
- As BPA levels have gone down, other bisphenols have gone up in proportion

Structural formula	Name
	Bisphenol A
	Bisphenol AP
	Bisphenol AF
	Bisphenol B
	Bisphenol BP
	Bisphenol C
	Bisphenol C 2
	Bisphenol E
	Bisphenol F
	Bisphenol G
	Bisphenol M
	Bisphenol S
	Bisphenol P
	Bisphenol PH
	Bisphenol TMC
	Bisphenol Z

Bisphenols & Cryptorchidism

- Plasma BPA, BPS & BPF significantly higher than control subjects.
 - BPA: median: 9.95 ng/mL vs. 5.54 ng/mL, $p < 0.05$.
 - BPS: median: 3.93 ng/mL vs. 1.45 ng/mL, $p < 0.001$.
 - BPF: median: 3.56 ng/mL vs. 1.83 ng/mL, $p < 0.05$.





Bisphenol Load Assessment

- Urinary BPA
 - Threshold: 3-5.0 ug/L (NO safe level)
- Million Marker Laboratory
 - <https://www.millionmarker.com>



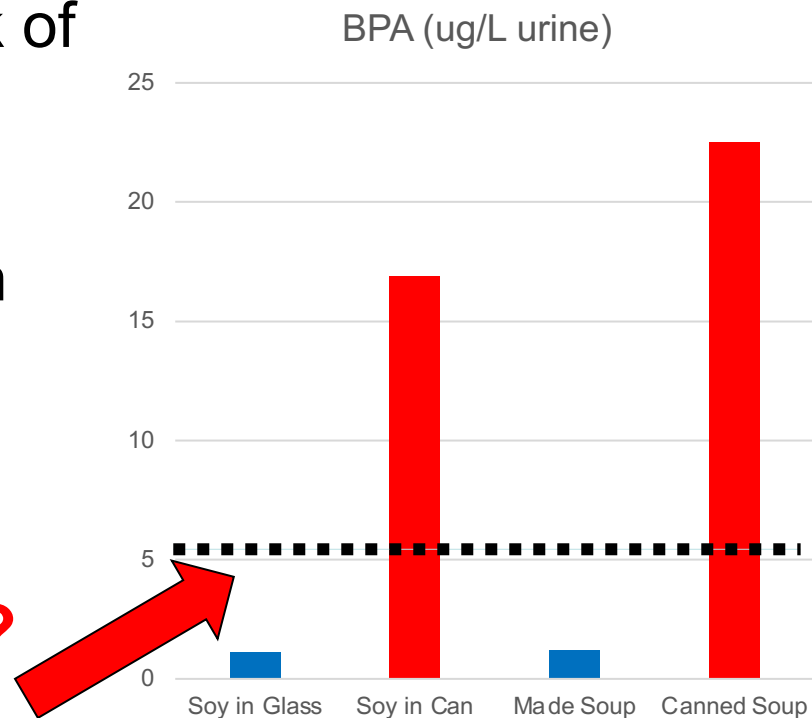
BPA Intervention

- Decrease exposure:
 - Clean house
 - Air filtration
 - Eliminate all plastic storage containers
 - Eliminate all canned food
 - Avoid touching thermal papers (e.g., receipts)
- Facilitate detoxification/excretion



Proper Containers/Storage Critical

- One 12oz serving daily for 1 week of either fresh soup or canned soup (Progresso)
 - 12-fold increase in BPA
- 2 servings of 6 ounces Soy milk in can compared to glass
 - 16-fold increase in BPA
 - Systolic BP elevated 4.5 mm Hg
- **Diabetes 2x risk threshold?**



Carwile JL1, Ye X, Zhou X, et al. Canned soup consumption and urinary bisphenol A: a randomized crossover trial. JAMA. 2011 Nov 23;306(20):2218-20.

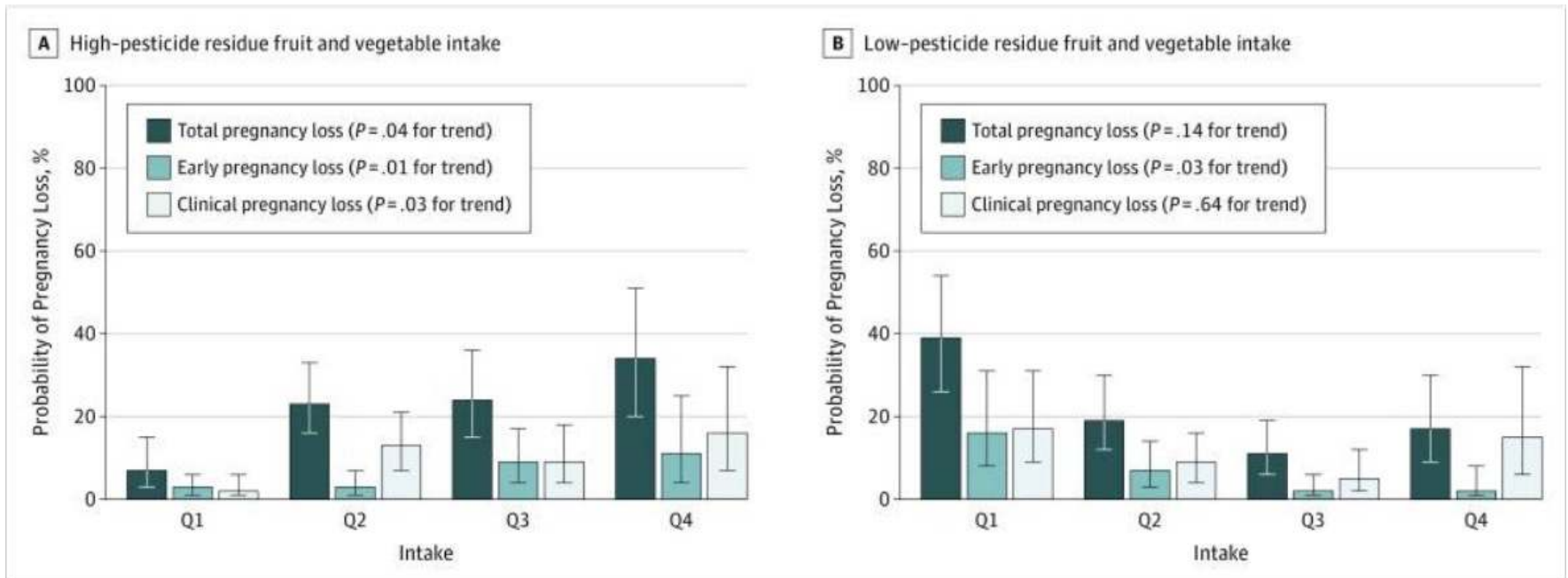
Bae S1, Hong YC2. Exposure to bisphenol A from drinking canned beverages increases blood pressure: randomized crossover trial. Hypertension. 2015 Feb;65(2):313-9.



Pesticides



Effect On Fertility of High vs Low Pesticide Fruit and Vegetable Diet



Chiu YH, Williams PL, Gillman MW, Gaskins AJ, Mínguez-Alarcón L, Souter I, Toth TL, Ford JB, Hauser R, Chavarro JE; EARTH Study Team. Association Between Pesticide Residue Intake From Consumption of Fruits and Vegetables and Pregnancy Outcomes Among Women Undergoing Infertility Treatment With Assisted Reproductive Technology. *JAMA Intern Med.* 2018 Jan 1;178(1):17-26. PMID: 29084307



Common Agricultural Chemicals Devastating to Male Fertility

- Levels of several pesticides compared to sperm quality measures
- Highest versus lowest:
 - Alachlor: OR = 30.0
 - Diazinon: OR = 16.7
 - Atrazine: OR = 11.3



Percent of Ground Water Exceeding Atrazine Safety Standard

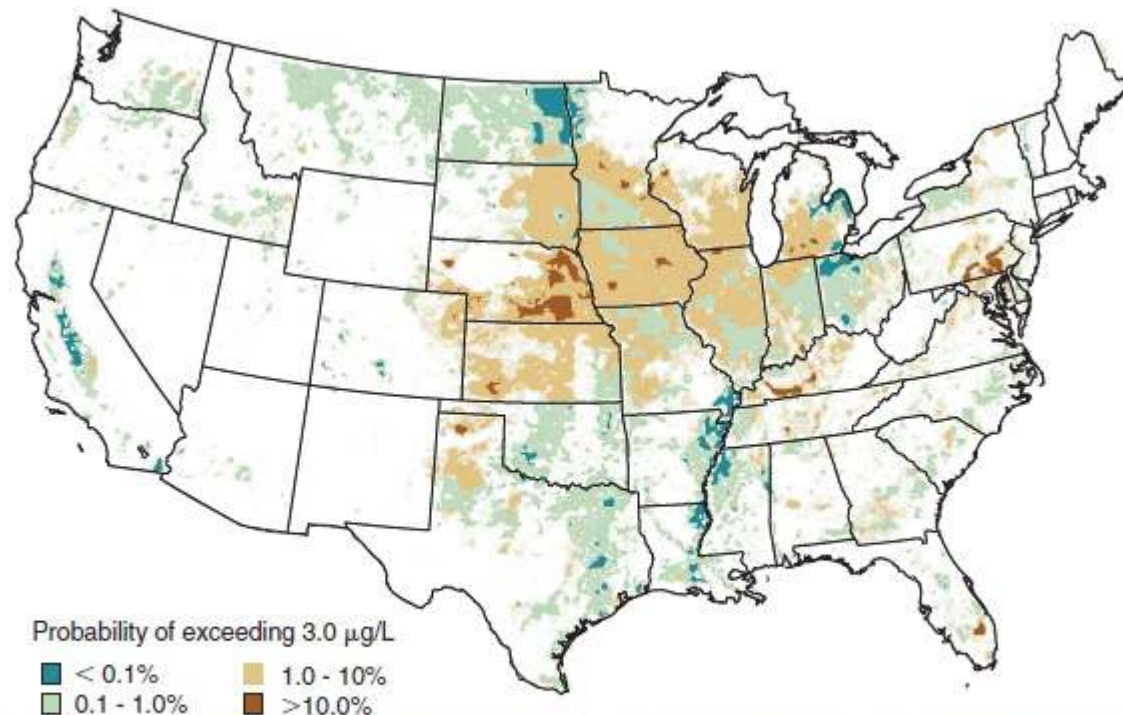


FIG. 4.7 Likelihood that atrazine plus deethylatrazine will exceed drinking-water standard in shallow groundwater underlying agricultural areas. (From U.S. Geological Survey. [2017]. *Pesticide national synthesis project*. Retrieved from <https://water.usgs.gov/nawqa/pnsp>)



B-Vitamin Deficiency Aggravates Pesticide Damage to Fertility

- Study of 291 women measured DDT and B-vitamins: folate, B6, B12
- Adequate levels of B-vitamins resulted in no correlation with DDT levels
- Women in top quartile of DDT AND bottom quartile of B12 suffered 56% decrease in fertility

25411282



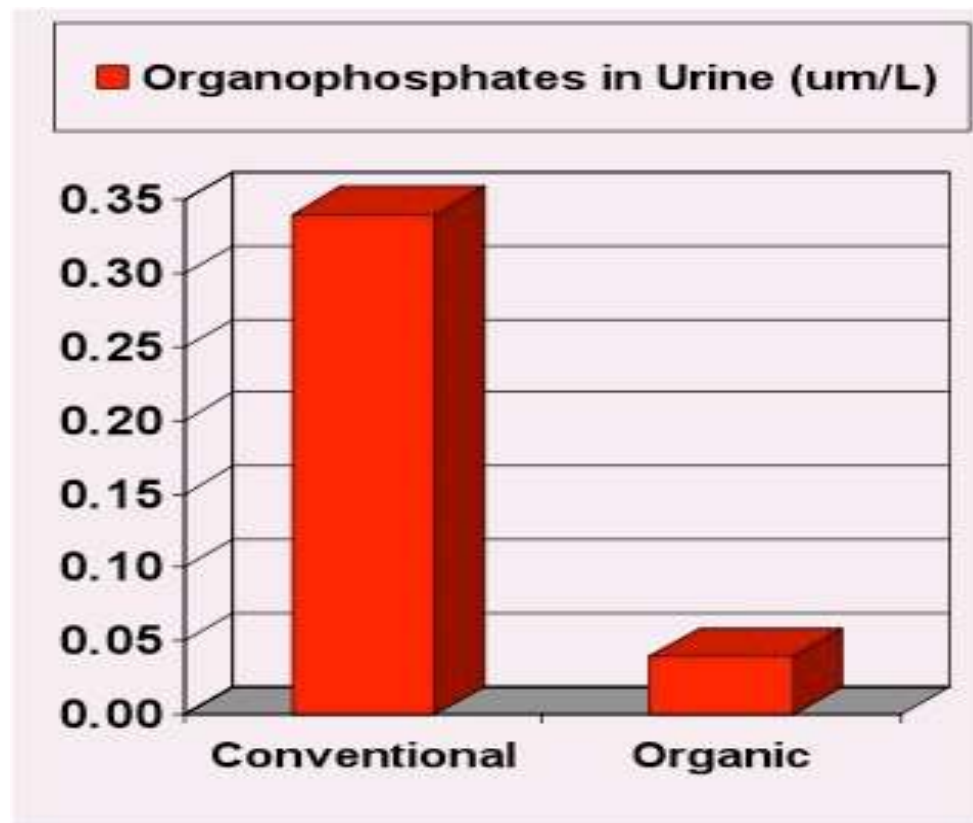
Pesticide Assessment

- Organophosphates
 - Great Plains Laboratory



Pesticide Reduction

- Eating organically decreases blood and urine levels quickly--measurable within 3 days
- This study done with children in Seattle

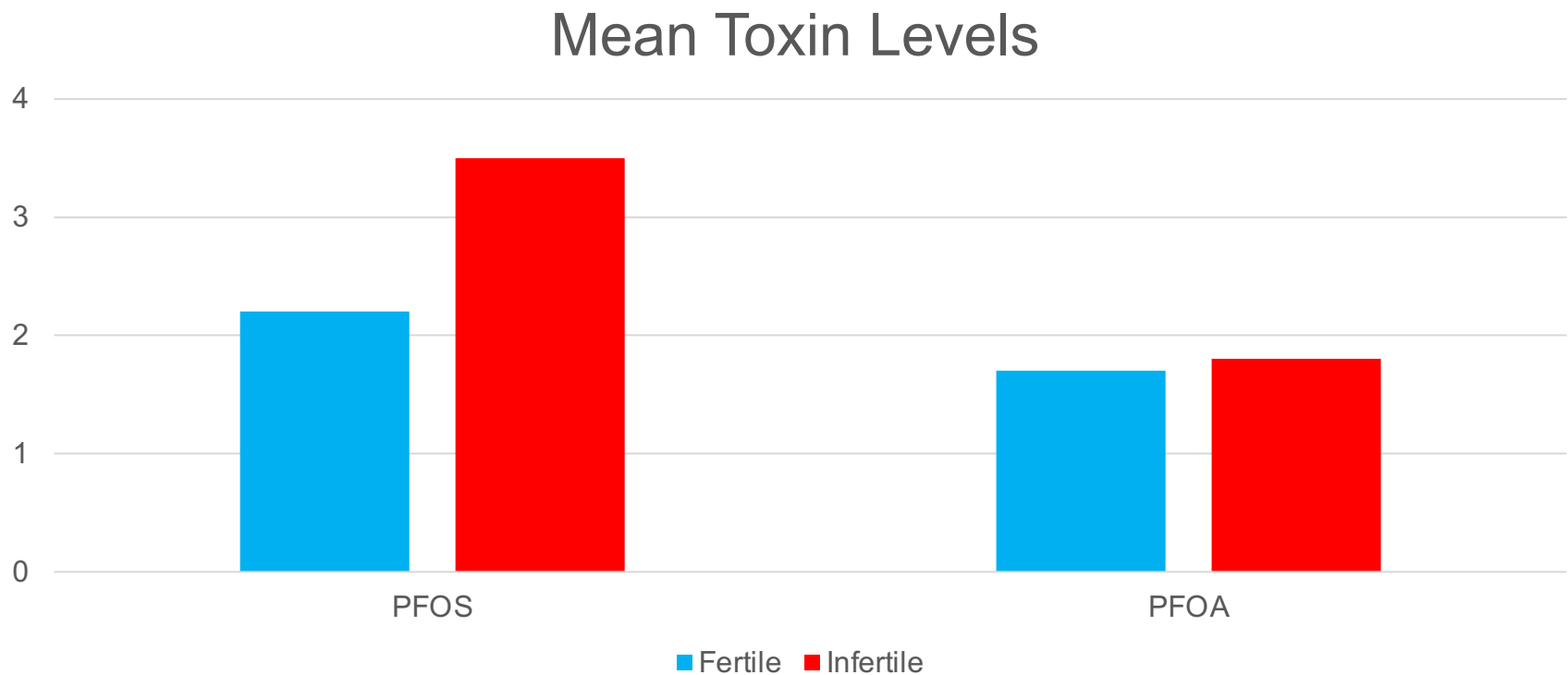




PFOAs



PFOAs Higher in Infertile Women





Decreasing PFOAs Improves Fertility

- Drinking water in Minnesota city highly contaminated with PFOAs
- Substantial decrease in fertility and birth size and increase in pre-term and
- Cleaning up the water supply resulted in substantial improvement in fertility
- Before compared to after water filtration:
 - Fertility: OR = 0.73
 - Low birth weight:: OR = 1.36
 - Premature: OR = 1.14

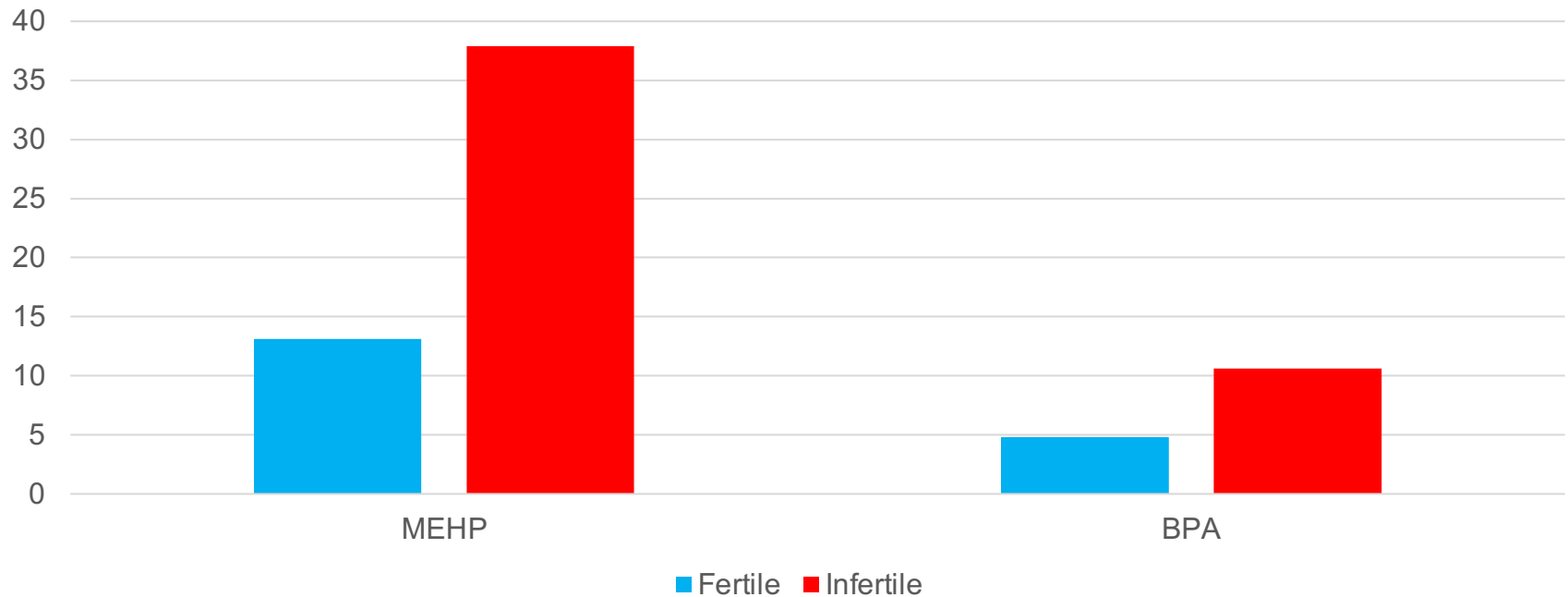


Phthalates



Phthalates Higher in Infertile Women

Mean Toxin Levels



La Rocca C, Tait S, Guerranti C, et al. Exposure to endocrine disruptors and nuclear receptor gene expression in infertile and fertile women from different Italian areas. *Int J Environ Res Public Health*. 2014 Sep 29;11(10):10146-64. PMID: 25268510



Phthalate Load Assessment

- Urinary phthalates
 - Threshold: 10.0 ng/ml (NO safe level)
- Million Marker Laboratory
 - <https://www.millionmarker.com>



Intervention

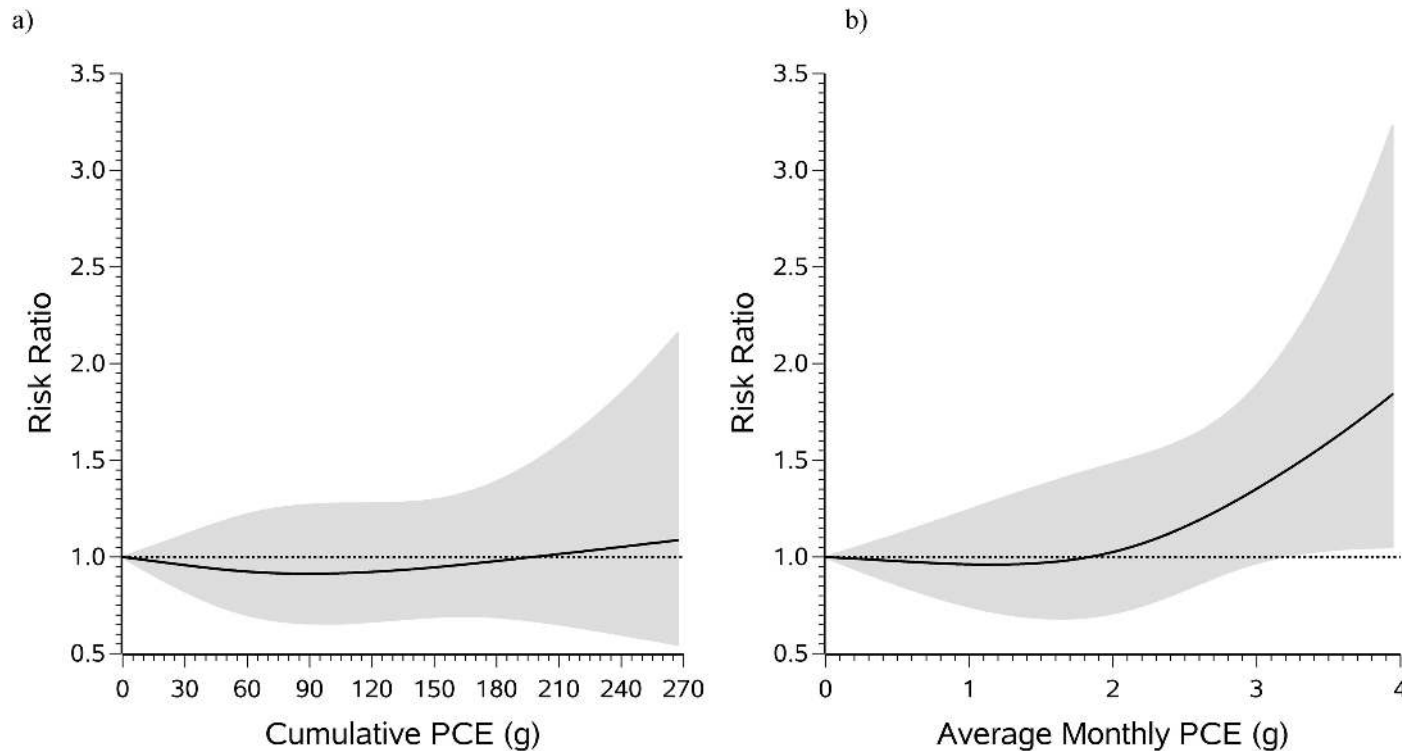
- Avoidance
 - Safe HABAs
 - Apps, like *Think Dirty*
 - Do not eat takeout foods in non-stick packaging
 - Etc.



Solvents



Regular Solvent Exposure More Damaging than Cumulative Exposure





Air Pollution

PM_{2.5}, PM₁₀, O₃, SO_x, NO_x

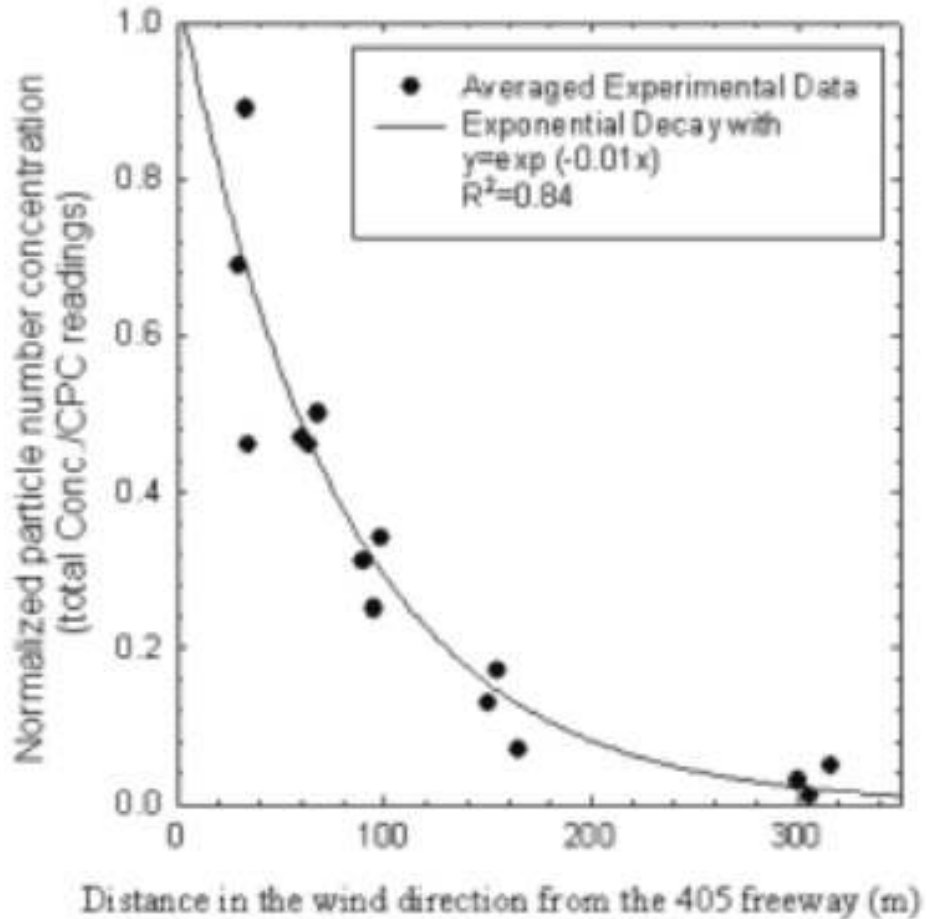


Common Air Pollutants Impair Many Aspects of Fertility

- Comprehensive review using both animal and human data
- Air pollution significantly:
 - Decreases spontaneous fertility
 - Decreases spermatogenesis
 - Increases oxidative damage to sperm DNA
 - Decreases ovarian function
 - Increases number of anovulatory cycles
 - Decreases success of IVF



PM According to Distance from Highway





PM/PAH Intervention

- Decrease exposure
 - Do not smoke
 - Limit charbroiling food
 - Move away from highways
 - Do not use diesel vehicles
 - **Air purifiers:**
 - Whole house: at least MERV-8 filter (prefer Merv-16)
 - Individual rooms: HEPA filters
- Support normal detoxification/excretion
 - Broccoli (cabbage family foods)
 - Curcumin
- Protection from damage
 - Antioxidants: Vitamins C and E
 - Fruits and vegetables
 - Fish oils



Strategies - Air

- Whole house filter: Merv-8 (at least), run 24/7
 - If not: HEPA filters in main rooms
- Take off shoes before entering house
- Declare scent-free zone
- Filter outdoor air for fresh circulation
- Toxin-absorbing plants decrease chemicals in air





Just 2 Days in Clean Room Improves Cardiac Measures

- Merv-12 filter
- 33-58% reduction in inflammatory mediators
- Decrease in blood pressure

TABLE 33.3 Reduction in Blood Pressure and Inflammatory Markers After 48 Hours of Residence in a Room with a MERV 12 Filter Unit

Cardiovascular	Biomarkers
Systolic pressure – avg. 2.7 mm Hg drop	IL-1B – 58% reduction
Diastolic pressure – avg. 4.8% mm Hg drop	Soluble CD40 ligand – 55% reduction
Exhaled nitrous oxide – 17% drop	Myeloperoxidase – 33% reduction
	Monocyte chemoattractant protein 1–17.5% reduction

Data from Chen, R., Zhao, A., Chen, H., Zhao, Z., Cai, J., Wang, C., et al. (2015). Cardiopulmonary benefits of reducing indoor particles of outdoor origin: a randomized, double-blind crossover trial of air purifiers. *Journal of the American College of Cardiology*, 65(21), 2279–2287.



PORTION OF INFERTILITY DUE TO TOXINS

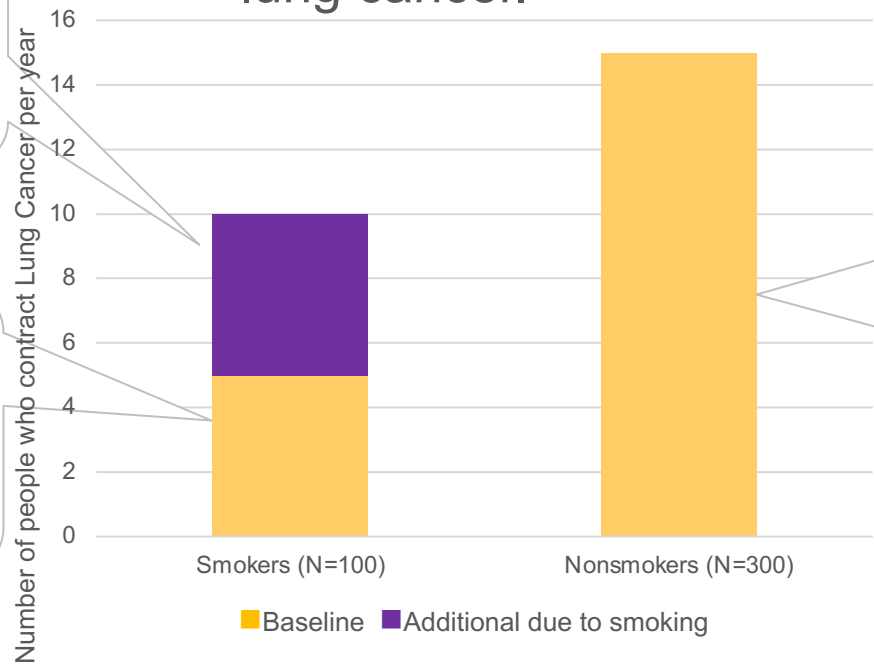


Example: Smoking and Lung Cancer

Number of smokers and nonsmokers who contract lung cancer.

A = 5
Number of smokers who contract Lung Cancer due to smoking

B = 5
Number of smokers who contract Lung Cancer not due to smoking



C = 15
Number of nonsmokers who contract Lung Cancer

$$AF = \frac{A}{A + B + C}$$

Rosen L. An Intuitive Approach to Understanding the Attributable Fraction of Disease Due to a Risk Factor: The Case of Smoking. Int. J. Environ. Res. Public Health 2013, 10, 2932-2943



Infertility, Male (1)

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
Parabens	10.66 ng/mL	25%		FR = 0.21	25767892
PCBs				FR = 0.62-0.78	23151773.
Phthalates				FR = 0.77-0.82	24534276
Lead				FR = 0.85	22309709
Sunscreen/personal care (2,2',4,4'-tetrahydroxybenzophenone = BP2); urine	0.1 ng/mL (75th percentile)			FR = 0.69	25395025



Infertility, Male (2)

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
Urinary pentavalent arsenate (Asi(V))	lowest quartile (0.2 ug/g Cr in control group; 7.8 among case group)	Upper 3 quartiles	8.4-36.5	Infertility	27485131
Trihalomethanes (chloroform)	Lowest tertile (blood) <12.3ng/L	Top 2 tertiles		Sperm count (reduced 17-22%)	31783240
PBDEs (BDE-47); hair	Median 9.4 ng/g. Risk expressed for every 10x increase			-19.7% sperm count, -25.5% motility	29684825
Perfluorinated compounds (semen)	Highest tertile (PFOA, 0.36 ng/mL) vs. lowest (043 ng/mL)			2.9–5.5% decreased sperm per log	31841032
Benzene (solvents)	Industrial (eg, pumping gas)			Sperm DNA damage	23422246
Organophosphate pesticides	Inverse correlation			Sperm count	25601731



Infertility, Male (3)

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
BPA (semen level)	44-94 pg/ml 98-205 69-228 84-330			Normospermic Oligospermic Teratospermic Azoospermic	26680493



Erectile Dysfunction

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
Benzene	Exposure		12.2		12065462
Organochlorine pesticides	Exposure		7.1		12065462
Smoking	Y/N	15%	1.7		12180231



Infertility, Female (1)

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
Organophosphate pesticides	Farming exposure			FR = 0.51-0.76	10069244
PCBs	Eating fish from Baltic vs Atlantic		2.5	FR = 0.54	10901111
Cadmium	Tertial	33.3%		FR = 0.78	22309709
Organochlorine pesticides (e.g. hexachlorobenzene, DDT, etc.)	β HCH lowest tertile <0.034 μ g/L; p,p'-DDE lowest tertile <0.026 μ g/L	Top 2 tertiles in French cohort		β HCH FR = 0.61 to 0.72; p,p'-DDE FR = 0.6 to 0.87	23348067
Perfluorinated compounds	1. PFOA median 1.7 ng/mL (maternal plasma) 2. PFOSA median 0.11 - 0.126 ng/mL (maternal serum)		1.3	1. FR = 0.89 - 0.91 per 1 SD increase 2. FR = 0.81 per 1 SD increase	25567616 23151773



Infertility, Female (2)

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
PBDEs	Mean BDE-17 = 0.0005 ng/g		1.2-1.3 per log in ng/g)	Pregnancy loss	30384231
Phthalates			2 to 3.4	Pregnancy loss while undergoing medically assisted reproduction	27299194
Ambient fine particles (PM2.5)	Mean of long-term PM2.5 = 11 µg/m ³	"AF ~72,000 per year in US."		FR = ↓ 0.7% per 5 µg/m ³ increase	30355539
Trihalomethane	80 µg/l water		1.4 3.2	Birth weight Cleft defects	
Perfluorinated			1.3		25567616
Mercury	Quartile	25%	1.04	1%	25127892
Benzene (solvents)	0.54 ng/mL in follicles			Decreased IVF success	24991235
Parabens (ethyl paraben)	Above detection level	96%	1.57	Infertility	32806428



Fetal Development Problems

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
Organophosphate pesticides		1 mile 8 mile	2.2 1.4	Fetal death	11246574
Arsenic	≥ 50 µg/L	1-3%	2.0 1.8	Spon. abortion Stillbirth	25626053
Smoking	Y/N		1.6-2.8	Preterm birth	14961888
Triazine herbicides			1.4 - 1.6	Lower weight and head size	8743439
CO, NO ₂ , O ₃ , PM _{2.5}			1.1-1.2	Lower weight and head size	22314199
BPA				Higher in fetuses with abnormalities	12401500
Cadmium	Maternal level			Lower weight and head size	27778365



IVF Failure

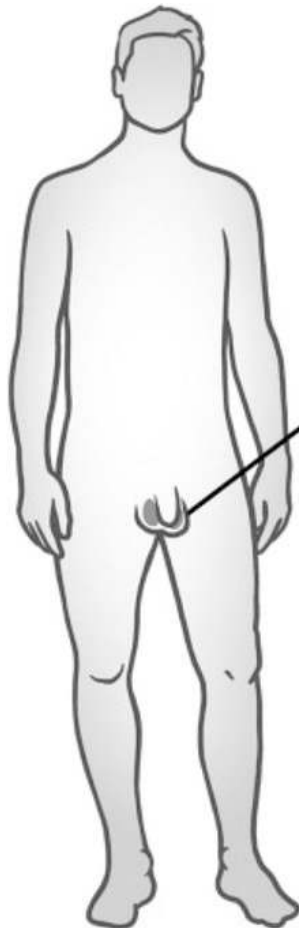
Toxin	Threshold	% Above Threshold	Odds Ratio	% of Disease	Example PMID
Parabens	10.7 ng/mL	25%		FR = 0.19	25767892
PBDEs	Detectable in follicular fluid	39%	10.0	FR = 0.22	22572111
Organochlorine pesticides	Quartile	25%		FR = 0.37-0.79	28089717
PCBs	Quartile	25%	1.7	Failed implantation	21345762
Benzene (solvents)	0.54 ng/mL in follicles			Decreased IVF success	24991235
BPA	Urine levels		Inversely proportional	# oocytes retrieved	20002217



Clinical Takeaways



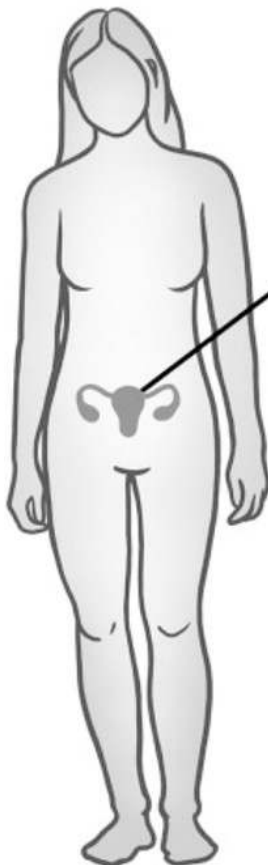
Summary Toxins Damaging Male Fertility



- BPA**
 - Reduced sperm concentration, motility, and normal morphology
- Phthalates**
 - Reduced fertility and semen quality parameters, but results are equivocal
- Air Pollution**
 - Reduced sperm motility
- Dioxins**
 - Reduced normal sperm morphology
- Pesticides**
 - Reduced sperm concentration, motility, and normal morphology
- Fracking Chemicals**
 - Reduced sperm concentration and motility
- Triclosan**
 - No definitive associations, further research is necessary
- Parabens**
 - Poorer fertility treatment outcomes in couples



Summary Toxins Damaging Female Fertility



BPA

- Disrupted cyclicity, fewer antral follicles
- Miscarriage, shortened gestation, preterm birth
- Poor fertility treatment outcomes
- PCOS, endometriosis, uterine fibroids

Phthalates

- Fewer antral follicles
- Shortened gestation, preterm birth
- PCOS

Air Pollution

- Preterm birth

Dioxins

- Reduced fetal growth

Pesticides

- Disrupted cyclicity
- Miscarriage, preterm birth
- PCOS, endometriosis, uterine fibroids

Fracking Chemicals

- Reduced fecundity
- Miscarriage, preterm birth

Triclosan

- No definitive associations, further research is necessary

Parabens

- No definitive associations, further research is necessary



Toxins Are Primary Drivers of Infertility

- Male sperm count and quality decrease in proportion to toxic load
- Female reproductive function impaired at every stage by many toxins
- Fetal viability inversely proportional to toxic load
- Environmental toxins also impair IVF
- Most toxins are avoidable
- Multiple methods to decrease toxic load



“The definitive book linking the exploding burden of environmental toxins to chronic diseases, including autoimmunity, obesity, and cancer.”

—MARK HYMAN, MD

THE TOXIN SOLUTION

How Hidden Poisons in the Air, Water, Food, and
Products We Use Are Destroying Our Health—
AND WHAT WE CAN DO TO FIX IT



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