Environmental Toxins and Neurodegeneration

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Potential Conflict of Interest

Dr. Pizzorno is Chair of the Science Advisory Board for Bioclinic Naturals

No Bioclinic Natural Products are recommended

Overview

1. Worldwide Epidemic of Brain Disorders
2. Toxins Damage Neurons and Brain Function
3. Methodology: Disease Risk to Disease Cause
4. The Worst Toxins
5. Sources of Toxins
6. Assessment of Toxin Load
7. Key Interventions
8. Case Histories

A Note About the Data

- All human data
- Primarily US as a lot more research available
- Spot checking toxins in other countries shows the same toxin overload, but variations in which are most prevalent:

  Australia (higher PDBEs)

  Canada (higher lead)

  New Zealand (higher cadmium)

  Sweden (higher most toxic metals)

  UK (highest PDBEs in world, 3x OCP of US)

Virtually every disease and clinical condition caused by neurological damage has increased in every age group the past 50 years

WHY?

Significant Clinical and/or Epidemiological Research Support for Neurotoxin Exposure

Diseases

- Attention deficit hyperactive disorder (ADHD)
- Autism spectrum disorder (ASD)
- Amyotrophic lateral sclerosis (ALS)
- Alzheimer's disease (AD)
- Parkinson's disease (PD)

Conditions

- Cognitive decline
- Dementia
- Headache
- IQ loss (esp children)
- Mood disorders
- Motor neuron disorders

Crinnion W, Pizzorno J. Neurotoxicity in, *Clinical Environmental Medicine*. Elsevier, 2018

The Worst Neurotoxins(?)

Prenatal

- Methylmercury
- Organophosphate pesticides
- PCBs
- Phthalates
- Polyfluoroalkyl chemicals

Postnatal

- Arsenic
- Cadmium
- DDT/DDE
- Lead
- Mercury
- OCPs
- PCBs
- Particulate matter (Vehicular exhaust)

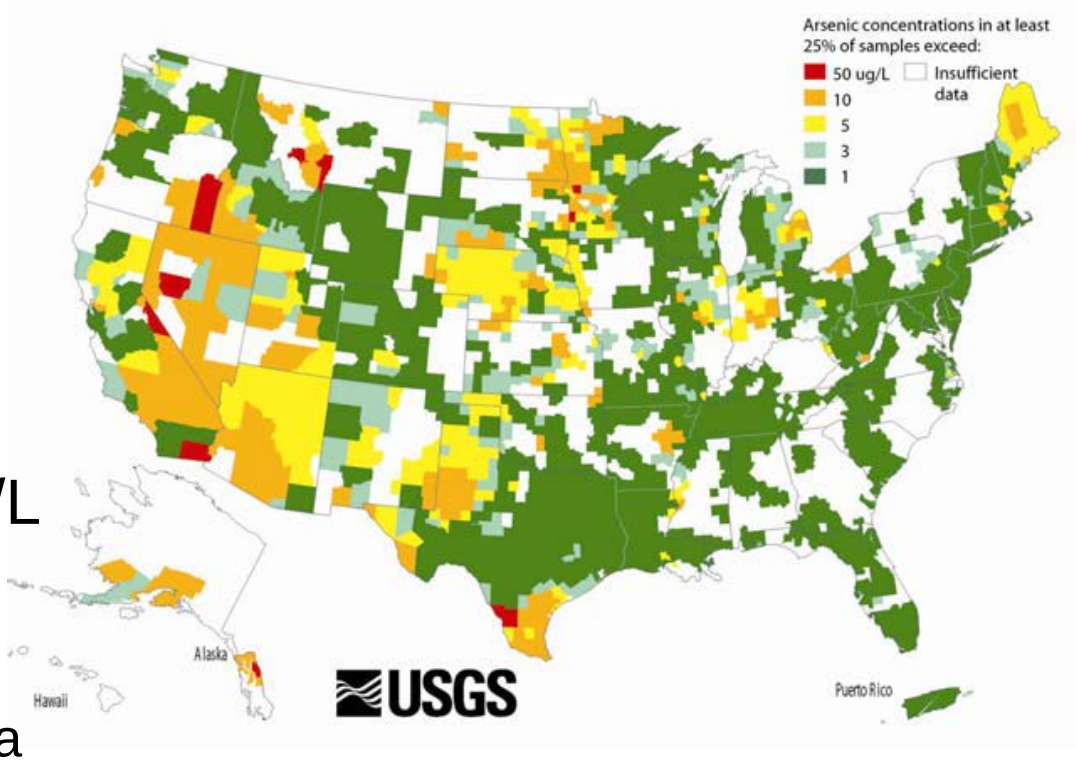
Primary Mechanisms of Neuron Damage

1. Oxidative stress
2. Inappropriate microglial activation
3. Mitochondrial damage
4. Methyl group depletion
5. Decreased production of BDNF

SOURCES OF NEUROTOXINS

Daily Arsenic Exposure Common

- <50% of US water supplies tested
- Average US water supply = 1 ug/L
- >10 ug/L increases risk of many diseases
- >10% of public water supplies has As >10 ug/L
- Some:
  - Maine wells 3,100 ug/L!
  - Similar to Taiwan & China



http://www.atsdr.cdc.gov/csem/arsenic/docs/arsenic.pdf (accessed 2015-08-18)
https://link.springer.com/article/10.1007/s40572-014-0012-1 (accessed 2017-03-30)
Neilsen MG, Lombard PJ, Schalk LF. Assessment of arsenic concentrations in domestic well water, by town, in Maine, 2005-2009. U.S. Geological survey Scientific Investigations Report 2010-5199.

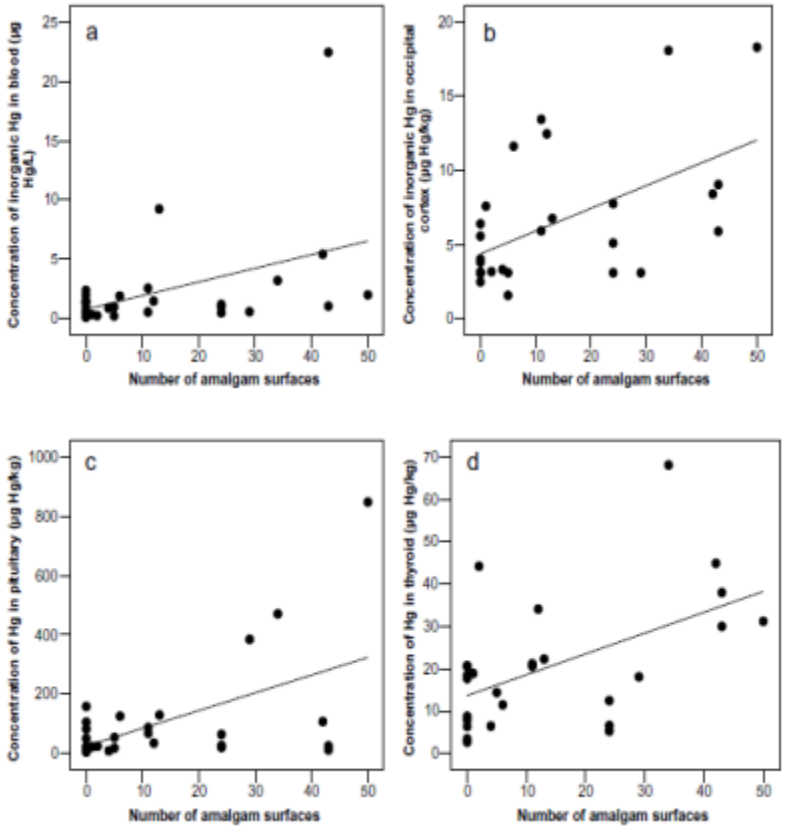
Mercury Exposure Common

- Average exposure in non-industrial populations
  - Amalgams: 10 ug/d
  - Fish: 2.3 ug/d
  - Water: 0.3 ug/d
  - Air
  - Vaccinations
- Industrial

Vimy, M.J., and Lorscheider, F.L (1990) Dental amalgam mercury daily dose estimated from intra-oral vapor measurements: A predictor of mercury accumulation in human tissues.]. Trace Elem. Exp. Med 3, 111-123

Amalgams Put Mercury Into the Brain

- **Mercury accumulates in the brain in proportion to surface area of amalgams**
- Study of 18 cadavers
  - Hg in brain, thyroid and kidneys proportional to the number of amalgam surfaces
  - For those with more than 12, Hg in brain disproportionately higher
  - Suggests that at higher levels of exposure the brain's mercury excretion pathways become overloaded.



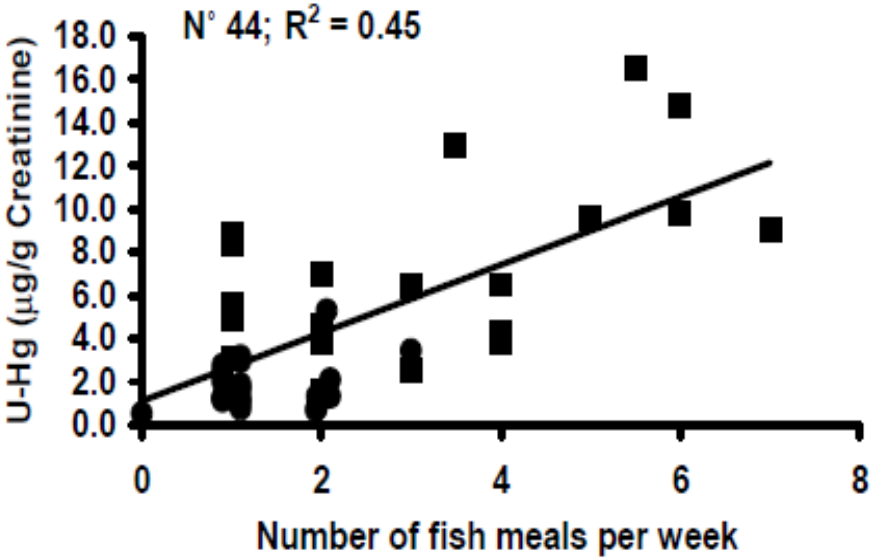
Guzzi 2006

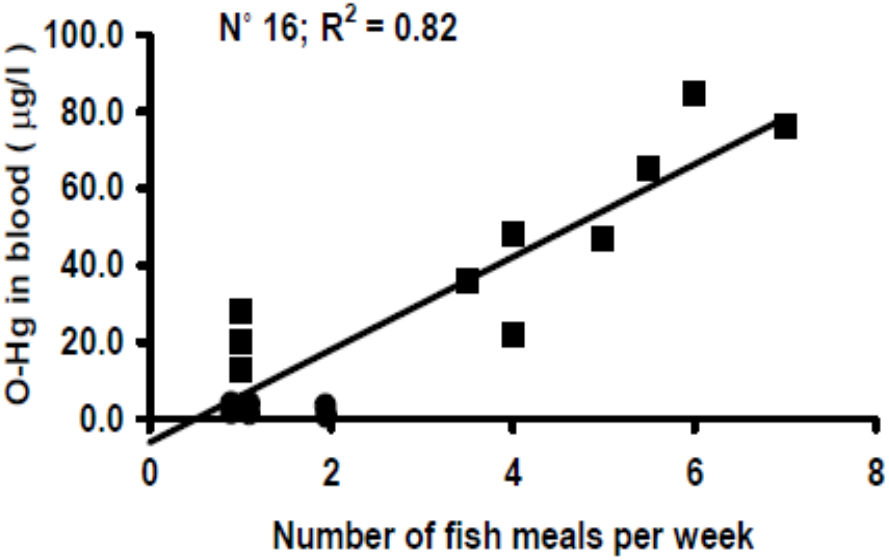
Reinhardt JW. Side-Effects: Mercury contribution to body burden from dental amalgam. Adv Dent Res. 1992;6: 110

Guzzi G, et al. Dental amalgam and mercury levels in autopsy tissues. Am J Forensic Med Pathol. 2006 Mar;27(1):42-5

Hg From Fish

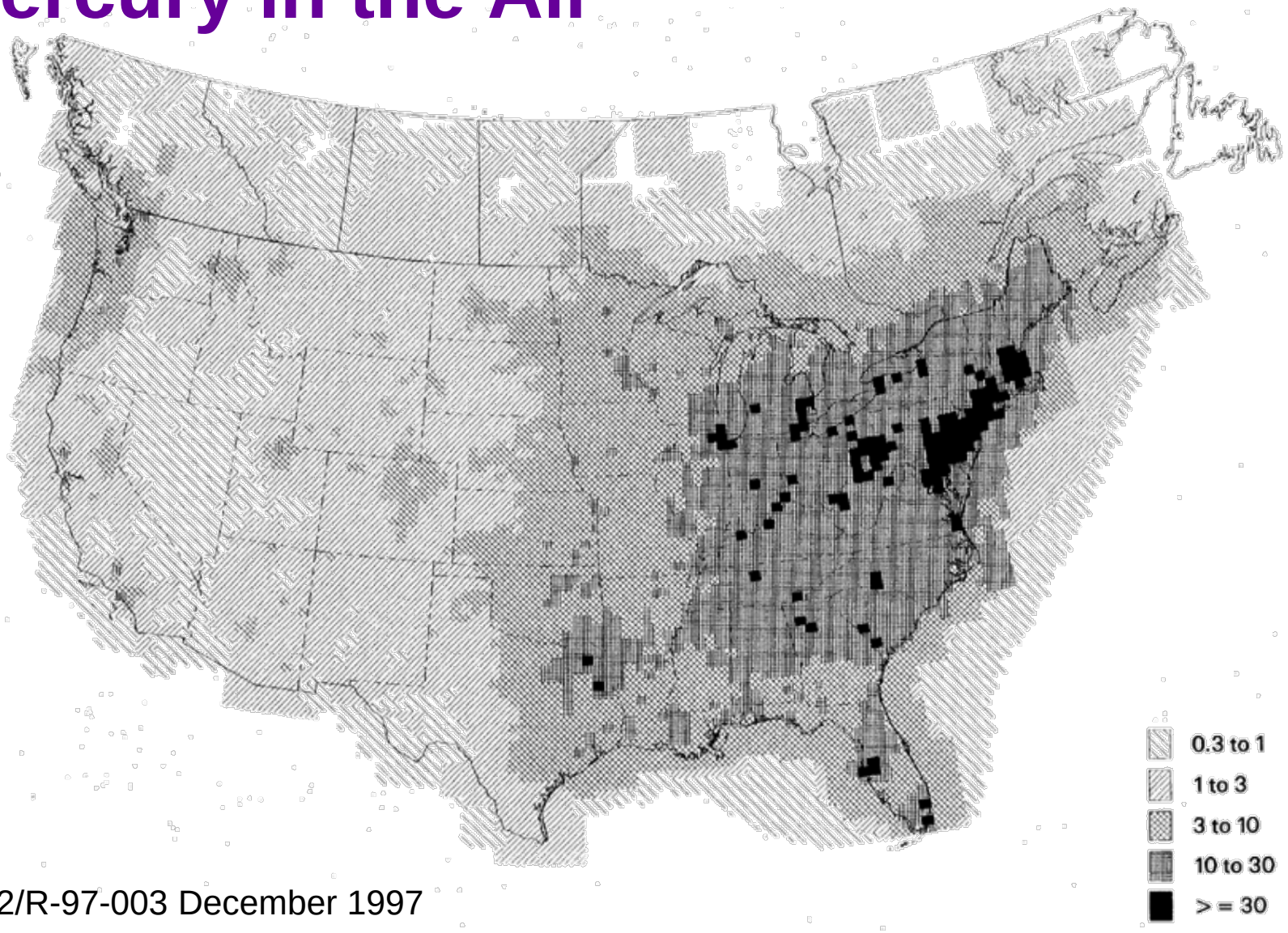
- **Total Hg urinary excretion proportional to amount of fish eaten**
- **Impaired psychomotor performance**
  - R = 0.38 blood
  - R = 0.77 urine
- Huge variation in amount of Hg in fish





Apostoli P, ICortesi I, Mangili A, et al. Assessment of reference values for mercury in urine: the results of an Italian polycentric study. The Science of the Total Environment 289 (2002)13-24
Carta P, et al. Sub-clinical neurobehavioral abnormalities associated with low level of mercury exposure through fish consumption. NeuroToxicology 24 (2003) 617–623

Mercury in the Air



EPA-452/R-97-003 December 1997

Mercury Neurological Symptoms

Effects of occupational exposure to mercury vapour on the central nervous system 549

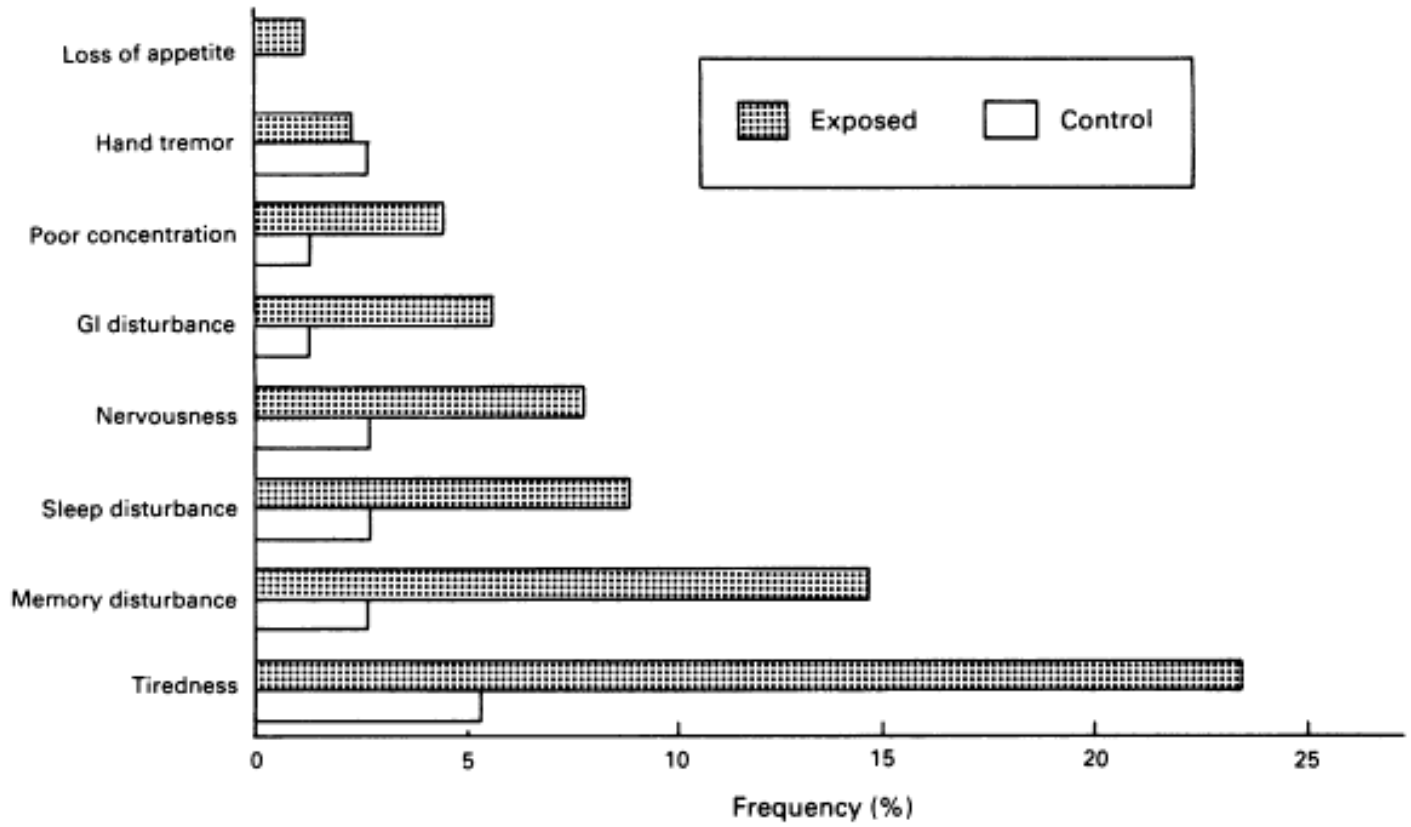


Figure 1 Symptom frequency in exposed and control groups.

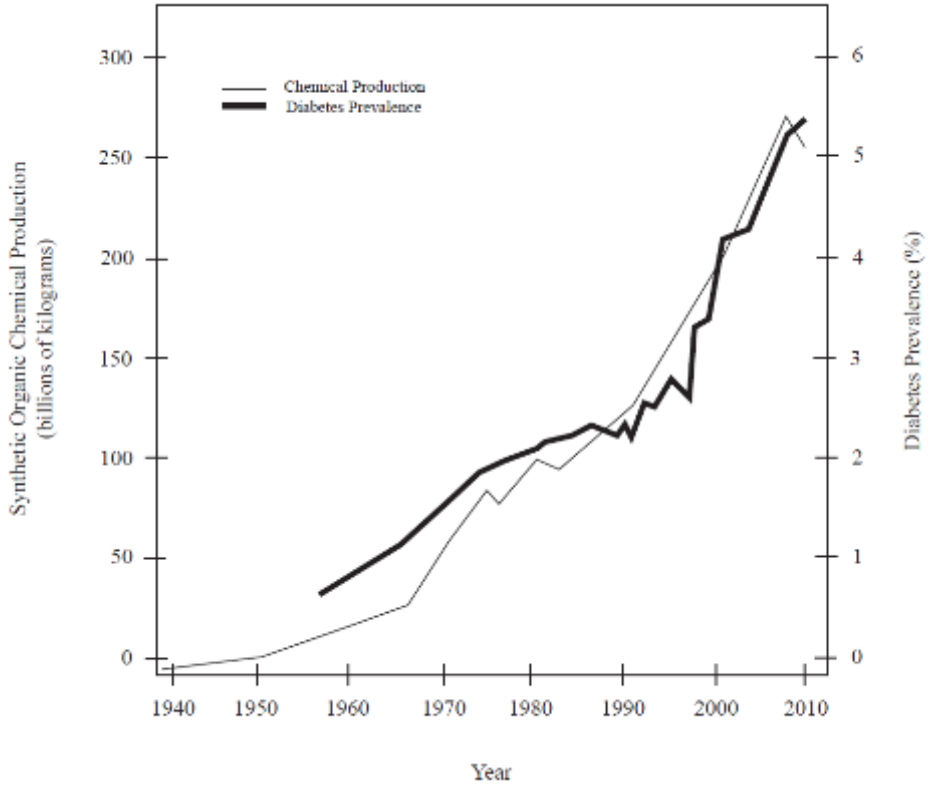
Langworth S, Almkvist O, Söderman E, Wikström BO. Effects of occupational exposure to mercury vapour on the central nervous system. Br J Ind Med. 1992 August; 49(8): 545–555

Persistent Organic Pollutant (POPs)

Chemical	Abbr.	Uses	Exposure
Bisphenol A	BPA	Plastics, can lining	Canned food
Organochlorine pesticides	OCPs	Pesticide	Food, fumigation
Organophosphate pesticides	OPPs	Pesticide	Food
Polybrominated diphenyl ethers	PBDEs	Flame retardant	Clothing
Polychlorinated biphenyls	PCBs	Industrial	Everywhere
Perflourinated	PFOAs	Non-stick, stain prevention, water repellant	Teflon, Gortex, Scotchguard
Phthalates		Plastics, fragrances	Shower curtains, cosmetics

Persistent Organic Pollutant Production

- Designed to be difficult to breakdown by biological processes
- Many neurotoxic
- Accumulate in humans with age
- Interfere with neurogenesis



Neel BA, Robert M. Sargis RM. The paradox of progress: Environmental disruption of metabolism and the diabetes epidemic. DIABETES, 2011; 60:1838-48

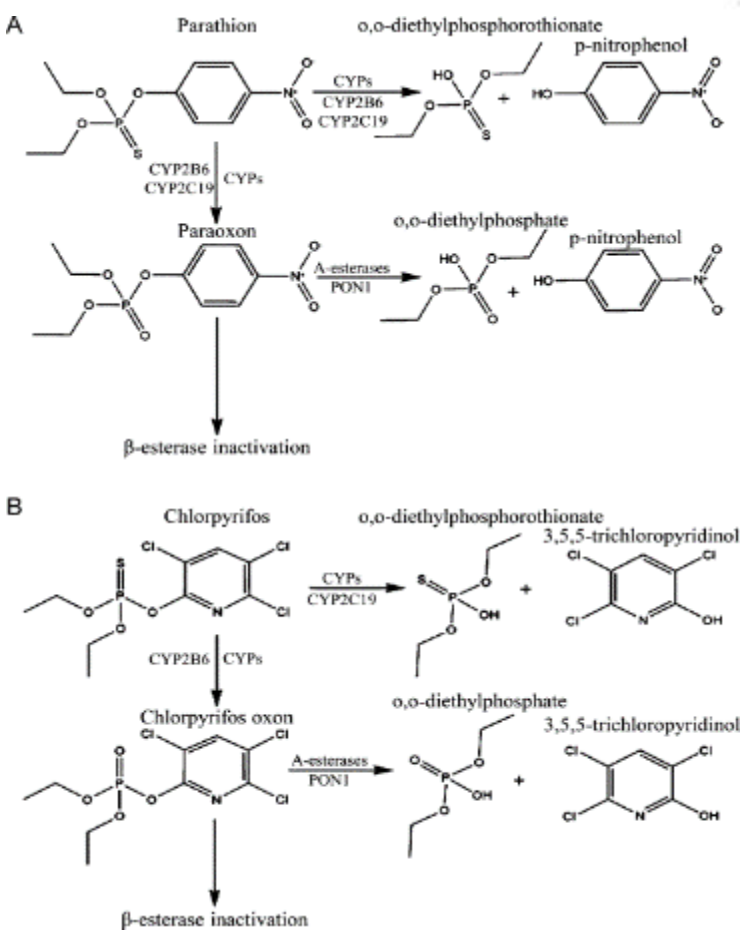
Weiss B. Endocrine disruptors as a threat to neurological function. J Neurol Sci. 2011;15:11-21.

Weisskopf MG, et al. Persistent organochlorine pesticides in serum and risk of Parkinson disease. Neurology. 2010 Mar 30;74(13):1055-61.

NEUROTOXICITY

POPs – Prenatal Effects

- Prenatal exposure particularly harmful - 3 studies
  - Higher levels of OP metabolites associated with poorer cognitive scores, (memory, processing speed, comprehension, and perceptual reasoning).
  - **Average deficit in IQ of 7 comparing highest to lowest quintile.**
  - 25% of pregnant women in US have levels exceeding the median in this study

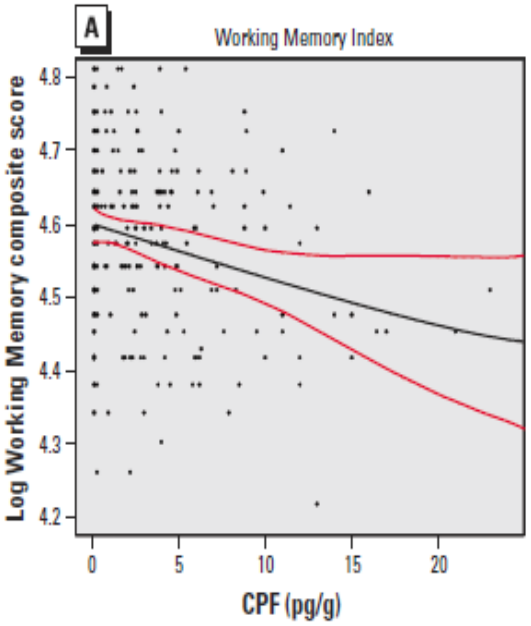


Foxenberg 2011 (21514354)

Bouchard MF, et al. Prenatal Exposure to Organophosphate Pesticides and IQ in 7-Year Old Children. Environ Health Perspect. 2011 Aug;119(8):1189-95

POPS – Prenatal Effects

- Higher maternal levels were associated with **decrease in total IQ of children 7 years later**, as well as working memory
- Most experts agree that working memory is related to a limited attention capacity.
- Children with higher levels of OP metabolites had up to **2x increased risk for ADHD**, and the levels associated with risk were commonly found in the US population among children.



Rauh et al. 2011

Rauh V, et al. 7-Year Neurodevelopmental Scores and Prenatal Exposure to Chlorpyrifos, a Common Agricultural Pesticide. Environ Health Perspect. 2011 Apr 21.
Bouchard MF,et al. Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides. Pediatrics. 2010 Jun;125(6):e1270-7.

POPS – Prenatal Effects

- Prenatal exposure to OPs also associated with cognitive impairment
- **Effect magnified in those with genetic variant for PON1 gene**, which reduces ability to detoxify chlorpyrifos
- **Same polymorphism increases risk for Parkinson's** disease when exposed to OP pesticides
- **Nearly 100% of US homes sampled had detectable OP and other pesticides on their floors**

Engel SM, et al. Prenatal Exposure to Organophosphates, Paraoxonase 1, and Cognitive Development in Childhood. Environ Health Perspect. 2011 Apr 21
Manthripragada AD et al. Paraoxonase 1, agricultural organophosphate exposure, and Parkinson disease. Epidemiology. 2010 Jan;21(1):87-94.
Stout DM 2nd, American Healthy Homes Survey: a national study of residential pesticides measured from floor wipes. Environ Sci Technol. 2009 Jun 15;43(12):4294-300.

Chlorpyrifos (CPF) & Brain Anomalies

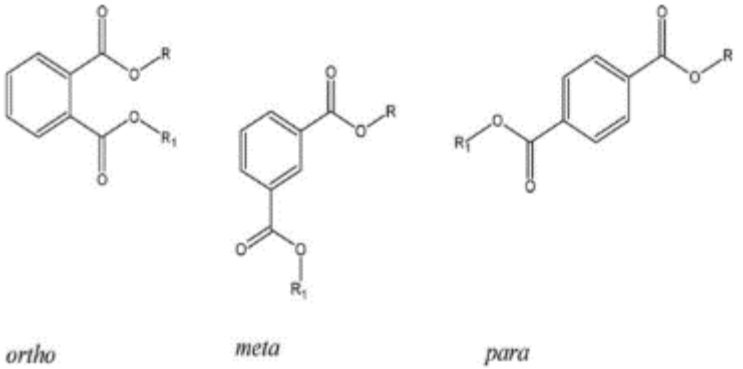
- Prenatal exposures to CPF and other OP pesticides linked to **smaller head size, lower birth weight, abnormal neonatal reflexes, and attention problems**
- Recent study found prenatal CPF exposure at high but routine levels had measureable effects on brain structure in children (MRI)
  - Random sample from Cincinnati blood bank during same time period had levels 2x as high in adults
- Affected areas involved in **attention and receptive function, social cognition, reward, emotion, and inhibitory control as well as executive functioning** – changes documented in size & morphology
- Those with high exposure also had **disruption in normal sex-specific brain differences**
- Exposure x IQ interaction – normal positive associations between surface area of some areas and IQ were not found in high exposure group
- Persistence of effects suggests they are irreversible

Rauh VA, et al. Brain anomalies in children exposed prenatally to a common organophosphate pesticide. Proc Natl Acad Sci U S A. 2012 May 15;109(20):7871-6. doi: 10.1073/pnas.1203396109

Polyfluoroalkyl Chemicals - Children

- **Developmental neurotoxicants**
- Associated with ADHD in children age 12-15
- **Eliminated very slowly from the body – serum ½ life of 2 to 8.5 years**
- **Gore-Tex, Scotchgard and STAINMASTER** all PFCs
- Serum levels directly associated with income (opposite of BPA, with higher levels seen in lower income)

Hoffman K, et al. Exposure to polyfluoroalkyl chemicals and attention deficit/hyperactivity disorder in U.S. children 12-15 years of age. Environ Health Perspect. 2010 Dec;118(12):1762-7.
Nelson JW, et al. Social disparities in exposures to bisphenol A and polyfluoroalkyl chemicals: a cross-sectional study within NHANES 2003-2006. Environ Health. 2012 Mar 6;11:10.



Fabjan et al. 2006 (17050082)

Phthalates

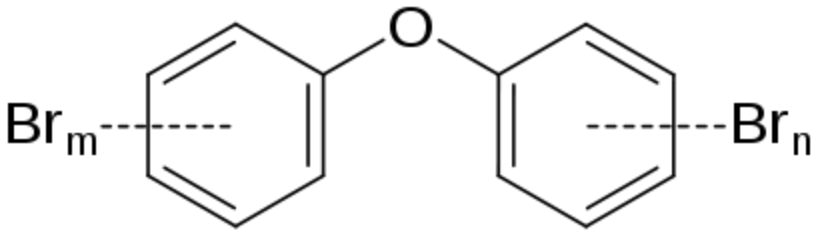
- Found in building materials, **personal cosmetics, pharmaceuticals, nutritional supplements**, solvents, adhesives, paints, lacquers, insecticides, air fresheners, shampoos, cleaning materials, **children's toys**, and **food packaging**
- May be listed as "**fragrance**"
- Dietary sources – chickens and eggs had DEHP metabolites, suggesting **chickens** (vs. packaging) are contaminated
- More than 75% of the U.S. population has measurable levels of several phthalate metabolites in the urine

Schettler T. Human exposure to phthalates via consumer products. Int J Androl. 2006 Feb;29(1):134-9;
Colacino JA, et al. Dietary intake is associated with phthalate body burden in a nationally representative sample. Environ Health Perspect. 2010 Jul;118(7):998-1003.

Phthalates are Endocrine and Neurological Poisons

- Prenatal exposure associated with **conduct & attention disorders**
- Act as anti-androgens, and endocrine disruptors
  - **Inverse relationships between urinary DEHP metabolites and total T4, free T4, total T3, and thyroglobulin**
  - Positive relationships with TSH
  - Associated with both diabetes prevalence as well as insulin secretion & resistance
  - Longitudinal study in children - higher urinary phthalate excretion associated with lower adrenal androgens in girls and boys (age 11), and higher testosterone in boys (age 13).

Engel SM, et al. Prenatal phthalate exposure is associated with childhood behavior and executive functioning. Environ Health Perspect. 2010 Apr;118(4):565-71.
Meeker JD, et al. Relationship between Urinary Phthalate and Bisphenol A Concentrations and Serum Thyroid Measures in U.S. Adults and Adolescents from NHANES 2007-08. Environ Health Perspect. 2011 Jul 11.
Lind PM, et al. Circulating Levels of Phthalate Metabolites Are Associated With Prevalent Diabetes in the Elderly. Diabetes Care. 2012 Apr 12.
Mouritsen A, et al. Urinary Phthalates from 168 Girls and Boys measured twice a year during a 5 Year Period: Associations with Adrenal Androgen Levels and Puberty. J Clin Endocrinol Metab. 2013 Jul 3.



PBDE – The New PCBs

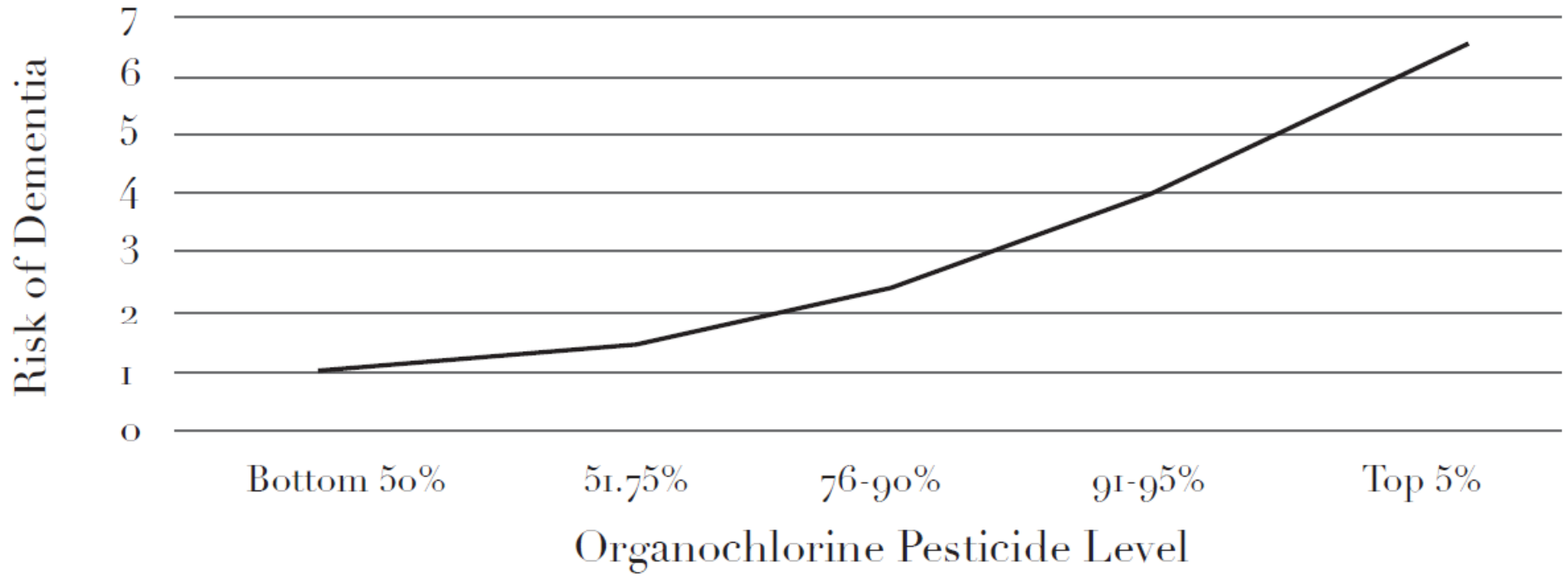
- Polybrominated diphenyl ethers
- Breast milk samples found PBDEs replacing PCBs
  - 30% of mothers more PBDEs than PCBs, and 65% had 3-fold higher levels.
- **Prenatal exposure linked to lower IQ**, and lower scores on tests of physical and mental development at 12-28, and 72 months
- **Postnatal exposure linked to poor social competence and attention deficit** in 4 year old children

She J, et al. Polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in breast milk from the Pacific Northwest. Chemosphere. 2007 Apr;67(9):S307-17

Gascon M, et al. Effects of pre and postnatal exposure to low levels of polybromodiphenyl ethers on neurodevelopment and thyroid hormone levels at 4 years of age. Environ Int. 2011 Apr;37(3):605-11.

Herbstman JB, et al. Prenatal exposure to PBDEs and neurodevelopment. Environ Health Perspect. 2010 May;118(5):712-9

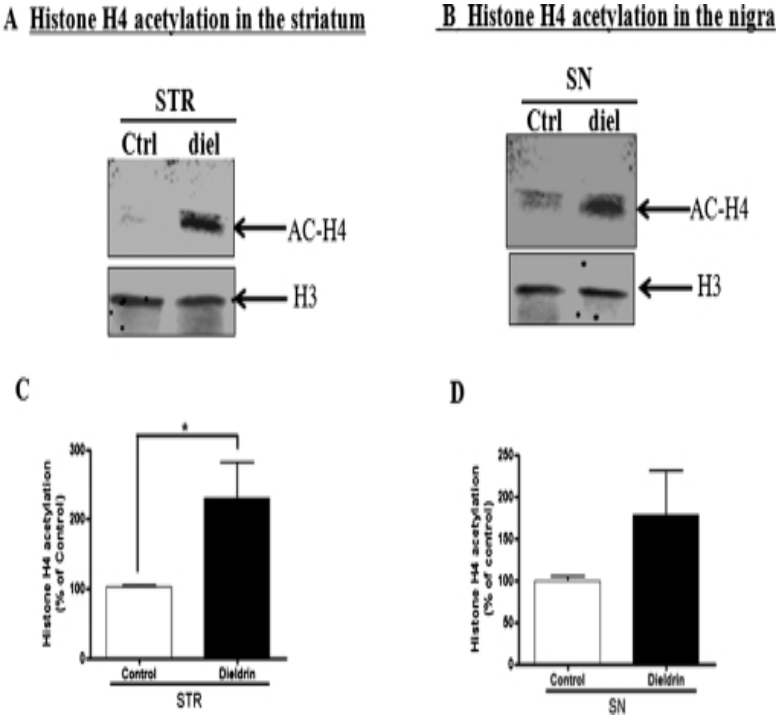
Organochlorine Pesticides and Dementia



Kim KS, Lee YM, Lee HW, et al. Associations between organochlorine pesticides and cognition in U.S. elders: National Health and Nutrition Examination Survey 1999–2002. Environment International 2015;75: 87–92

Parkinson's & Epigenetic Modulation

- Animal-based study: Dieldrin increases histones acetylation in dopaminergic neuronal cells,
  - It rapidly induces hyperacetylation of histones, as early as 10 min after the start of dieldrin exposure in dopaminergic neuronal cells
  - Long-term exposure also induces histone hyperacetylation in the striatum and substantia nigra
  - HAT inhibitor, anacardic acid had neuroprotective effect independent of antioxidant mechanism
  - Conclusion: "**hyperacetylation is an early signaling event in the execution of apoptosis after neurotoxic exposure to the environmental toxicant dieldrin**"



Song 2010

Song C, et al. Environmental neurotoxic pesticide increases histone acetylation to promote apoptosis in dopaminergic neuronal cells: relevance to epigenetic mechanisms of neurodegeneration. Mol Pharmacol. 2010 Apr;77(4):621-32.

Solvents Impair Neurological and Psychological Function

- Compared auto repair workers exposed 2.3 hr/day to those exposed most of day to toluene
- All wore face masks and protective gear
- **Impairment of sympathetic nerves** (OR = 4.1)
- **Impairment of peripheral nerves** (OR = 6.9)
- Positive relationship between **neurological abnormalities** and a self-reported **neuropsychiatric** measurement (r = 0.35-0.66)

Shih HT, et al. Subclinical abnormalities in workers with continuous low-level toluene exposure. Toxicol Ind Health. 2011 Sep;27(8):691-9

% OF CHRONIC DISEASE DUE TO NEUROTOXINS

Converting Disease Risk to % Caused: Attributable Fraction Calculation

$$AF = \frac{p(rr-1)}{p(rr-1)+1}$$

p = underlying prevalence of risk factor in the population

rr = relative risk (risk of contracting a disease in an exposed population divided by the risk of contracting the disease in an unexposed population)

AF = % of disease due to the identified cause

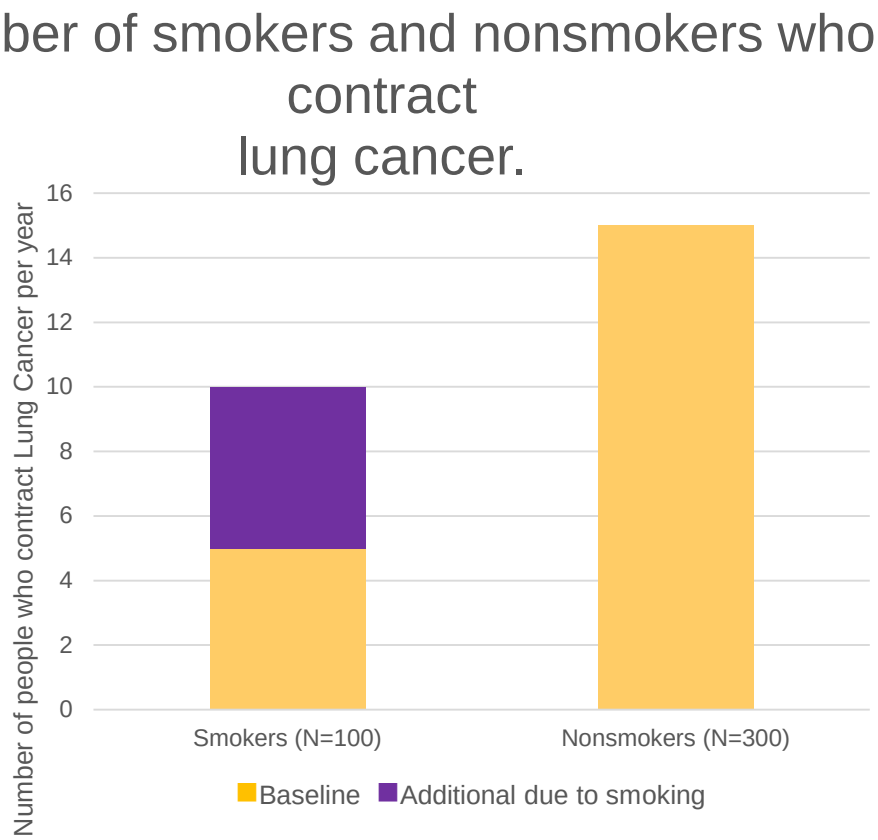
Levin, M. The occurrence of lung cancer in man. *Acta Unio Int. Contra Cancrum*. 1953, 9, 531-541

Example: Smoking and Lung Cancer

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

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

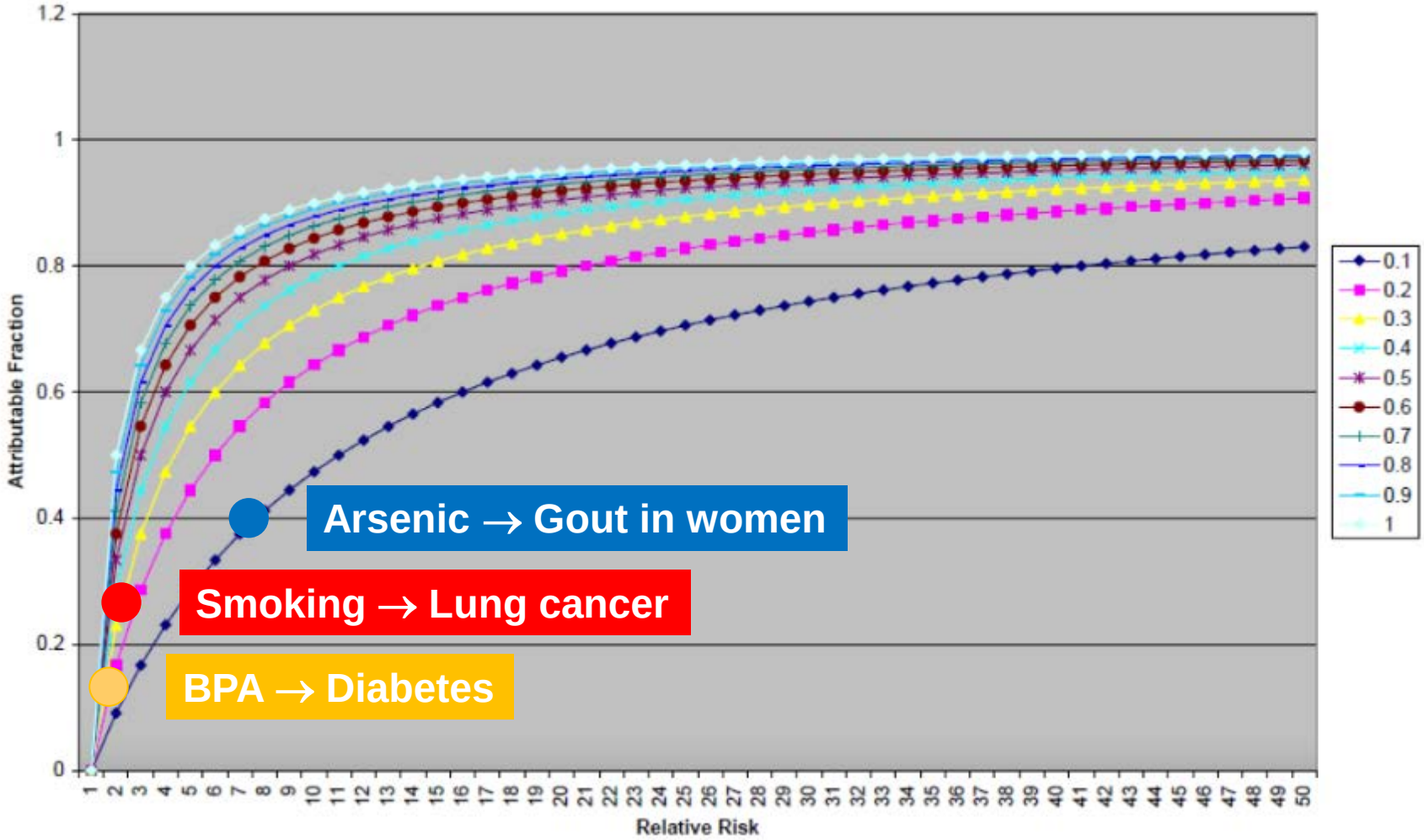
B = 5
Number of smokers who contract Lung Cancer not due to smoking



C = 15
Number of nonsmokers who contract Lung Cancer

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

AF, OR, Prevalence



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 Jul 16;10(7):2932-43

Our Process In Summary

1. Determine incidence of disease in “unexposed” population
2. Determine threshold for increased disease risk
3. Determine % of population above threshold
4. Determine incidence of disease (OR) in those above threshold
5. Calculate AF, i.e., % of disease

Whole population is exposed, so probably UNDERESTIMATES % of disease.

However, independence almost impossible, so OVERESTIMATES as well.

Status of Our Research

- 26 toxins and toxin classes, e.g. lead, mercury, BPA, OCPs
  - 100s of chemicals and POPs in some classes
- 18 cancers
- 24 chronic diseases

- 1,092 cells in spreadsheet

Large Personal Ongoing Research Investment

Huge Amount of Research Work!

	ADHD	Alzheimer's Disease	ALS	Angiosarcoma	Anxiety	Atopic Conditions	Cancer, Bladder	Cancer, Bone	Cancer, Brain	Cancer, Breast	Cancer, Cervix	Cancer, Colorectal	Cancer, Endometrial	Cancer, Head&Neck	Cancer, Liver	Cancer, Lung	Cancer, Lymphoma/neoplastic	Cancer, Ovarian	Cancer, Pancreatic	Cancer, Prostate	Cancer, Renal	Cancer, Skin	Cancer, Testicular	Cancer, Thyroid	Diabetes	Dyslipidemia	Gout	Hypertension	Infertility/Fetal Developmental Problems	Juvenile IQ	Juvenile Obesity	Metabolic Syndrome	Mitochondrial dysfunction	Myocardial Infarction	Obstructive Lung Disease	Osteoporosis	Peripheral Artery Disease	Peripheral Neuropathy	Prediabetes	Renal Disease	Rheumatoid Arthritis	Thyroid Dysfunction
Aluminum	N.D	1.99	Insufficient data	N.D	N.D	Insufficient data	N.D*	N.D	Insufficient data	Insufficient data	N.D	N.D	N.D	Insufficient data	N.D	N.D	Insufficient data	N.D	N.D	N.D		N.D	N.D		Insufficient data	mixed	N.D	N.D	No association/ 2.3*	theoretical	N.D	N.D	animal/in vitro evidence	N.D	only occupational	see renal dz					No association	N.D
Arsenic	Insufficient data	theoretical	Insufficient data	possible hepato	Insufficient data	Insufficient data	14.50%	Insufficient data	No association	Insufficient data	Insufficient data	gender-dependent	N.D	2.4*	No association	1.59	0.49	N.D	29%	31.20%	0.64	1.37	N.D		19%	1.10%	60.8% (women)	11.9% (men)	Insufficient data	0.5 gr dec	No association	Insufficient evidence	theoretical	Insufficient data/theoretical	No association	theoretical	Insufficient data	Insufficient data		More studies needed	Insufficient data	theoretical
Acrylamide	No assoc.	N.D		No assoc.			Not studied	Not studied	1	1	Not studied		1				2	1	1				1		Insufficient Evidence		N.D	N.D		N.D	N.D	N.D		N.D	N.D/ No available data			1				
Acrylonitrile	N.D	N.D																							N.D																	
Benzene	None	N.D	Insufficient data	animal evidence	N.D	Causes skin damage, but insuff data	No effect in animal model	N.D	N.D	1.91/insuff e/I	N.D	N.D	Insufficient data	N.D	N.D	Insufficient data	1.94	Insufficient data/animal data	One study available with no assoc.	No assoc. in animal model	N.D	N.D	N.D	More studies needed	N.D	N.D	N.D	N.D	See Comment	N.D	N.D	N.D			More studies needed	N.D		More studies needed	N.D	More studies needed	N.D	No Association
Bisphenol A	More studies needed	Hypothetical role - MGN				1.3				More Studies needed															13.91%				Insufficient data		2.22	1.51		Indirect animal evidence	1.3				1.34			
Cadmium	No assoc - limited data	Insufficient data																							More studies needed				Insufficient data					1.9	2.53	1.4				1.22		
Chloroform	N.D	N.D					1.4					1.53													Appears protective?										N.D							
DDT	19.90%	44.40%		N.D	N.D		No association	N.D	N.D	No assoc.; 2.07	N.D	likely assoc.	No association	N.D	2.9	1.7	1.2	N.D	2.9	No association		N.D	1.4-2.6		see dioxins		N.D	N.D			No association				1.97							
Dioxins	N.D	Theoretical															2.4								4.30%										More studies needed							
Fluoride	N.D	Unnoticed - dentistry		N.D			0.9	1	N.D	N.D	N.D		N.D												More studies needed							N.D	cell culture data	Insufficient data	More studies needed (1.1 to)	Weak animal assoc.					
Glyphosate	None	Theoretical	N.D	N.D	Insufficient data/theoretical		N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	More studies needed	N.D	N.D	N.D		N.D	N.D		Theoretical		N.D	N.D	Animal studies	N.D	N.D	N.D	cell culture data	N.D	N.D							
Lead	~1.7	Insufficient data	1.9	N.D					1.5																N.D		3.6-fold inc risk; see comment		See note	1-2 gr dec					2.37	1.11		See Comment	N.D	1.09	N.D	No association
Manganese	More studies needed	Possibly correlated																							More studies needed					0.7 gr dec				More studies needed; inversely assoc							
Mercury	1.9	Insufficient data																weak ass. data	N.D						More studies needed				0.99%					1.3				1.07		
Organochlorine pesticides	See PCB Data																								2.10%			2.5													
Organophosphate pesticides	2																								More studies needed					7.1 gain/dec											
Parabens	N.D			N.D			N.D	N.D	N.D	Insufficient data	N.D		N.D			N.D	N.D	N.D	N.D			theoretical assoc.	N.D		N.D		N.D	1	N.D	N.D	N.D	Insufficient data	N.D	N.D	N.D		N.D	N.D	N.D	N.D	N.D
Phthalates	2.30%	Possible correlation, more data needed								More studies needed					Probable										22.39%				Positive in animal studies					More studies needed - see note							
Polybrominated diphenyl ethers	19%	N.D														See note								No association	Insufficient data				May affect neurodevelopment											Insufficient data
Polycyclic aromatic hydrocarbons	19%	N.D	N.D	N.D	4.6	Positive correlation in animals/humans	1.4	N.D	See note	2.1				1.45		1.31	Possible (+) correl, more research needed	OR 1.2 in surrogate marker, more studies needed	Unknown assoc.	More research needed	No association	Positive in animals, highly adjusted	N.D		19.29%	1.39-1.99	No assoc.	N.D	Some effects in animals	0.1 gr dec			Positive correlation	N.D	N.D	N.D		N.D		N.D
PCBs	19%	More Studies needed		N.D			1.19-1.927	N.D	No stat-sig relationship	1.19-1.59	N.D		No assoc.			?	1.43	N.D	Insufficient data			No assoc.		13.10%		N.D	N.D		N.D	N.D	N.D		23.10%	No association	No assoc.		Assoc with toxic exp	N.D	Weak animal assoc.	9.5	
Vinyl chloride	N.D	N.D	More Studies Needed	I	N.D	See CDC Tox data - no stud data								See Angiosarcoma		1.3									N.D		N.D	N.D	Possible correlation - weak studies					N.D			Correlated				

Toxins Studied

Aluminum
Arsenic
Cadmium
Fluoride
Lead
Manganese
Mercury

Acrylamide
Acrylonitrile
Benzene
Bisphenol A (BPA)
Chloroform
DDT
Dioxins
Glyphosate
Organochlorine pesticides (OCPs)
Organophosphate pesticides
Parabens
Phthalates
Polybrominated diphenyl ethers (PBDEs)
Polycyclic aromatic hydrocarbons (PAHs)
Polychlorinated biphenols (PCBs)
Vinyl chloride

Diseases Studied

ADHD
Alzheimer's Disease
ALS
Angiosarcoma
Anxiety
Atopic Conditions
Diabetes
Dyslipidemia
Gout
Fetal Abnormalities
Hyperuricemia
Infertility
Juvenile IQ
Juvenile Obesity
Metabolic Syndrome
Mitochondrial dysfunction
Myocardial Infarction
Obstructive Lung Disease
Osteoporosis
Peripheral Artery Disease
Peripheral Neuropathy
Prediabetes
Renal Disease
Rheumatoid Arthritis
Thyroid Dysfunction
Cancer, Bladder
Cancer, Bone
Cancer, Brain
Cancer, Breast
Cancer, Cervix
Cancer, Colorectal
Cancer, Endometrial
Cancer, Head & Neck
Cancer, Liver
Cancer, Lung
Cancer, Lymph & Blood
Cancer, Ovarian
Cancer, Pancreatic
Cancer, Prostate
Cancer, Renal
Cancer, Skin
Cancer, Testicular
Cancer, Thyroid

How to Interpret the Following Slides

Threshold – Threshold exposure at which there is an increased risk of disease outcome

% Above Threshold – Percentage of the population with higher exposure than the threshold

Odds Ratio – Increased disease risk in those above threshold

% of Dz – Percent contribution of the toxin to that disease outcome

Attention Deficit Hyperactivity Disorder

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Dz	Reference PMID
DDT	1.26 ng/g serum (p,p'-DDE)	25.0%	1.8	16.6%	20106937
Lead	2.3 ug/dL	1.3%	2.54	2.0%	27659349
Mercury	~3.5ug/dL maternal whole blood	Difficult to determine, ~8-9%	1.6	Difficult to determine, 3.2%	24952233
Organophosphate pesticides	~413nm/L	NAD	1.55	NAD	20478945
Polycyclic Aromatic Hydrocarbons	2.27 ng/m3	94.0%	1.25	19.0%	22440811
PCBs	1.04 ng/g serum (sum of 50 PCBs)	25.0%	1.76	16.0%	20106937

Juvenile IQ

Toxin	Threshold	% Above Threshold	Odds Ratio	% of Dz	IQ Change	Reference PMID
Arsenic	>50ug/L urine	~5%	Reported as Beta	NAD	0.5 point decrease	23570911
Fluoride	0.7mg/L urine	NAD	Not Reported	NAD	0.59 point decrease per 1mg/mL fluoride	21237562
Lead	5-10ug/dL	~5%	Reported as Beta	NAD	4.9 point decrease	21450073
Organophosphates	75nmol/L	NAD	Reported as Beta	NAD	5.6 point decrease	21507776
PAHs	17.96ng/m3	NAD	Reported as Beta	NAD	3.8 point decrease	20406721
Phthalates	19.4 & 5.0 ug/L (MnBP/MiBP)	~41% ~57%	Reported as Beta	NAD	6.7-7.6 point decrease	25493564

Neurological Diseases—Adults

Disease	Toxin	Threshold	% Above Threshold	Odds Ratio	% of Dz	Reference PMID
Alzheimer's	Aluminum	0.1 mg/L drinking water	40%	2.0	~30.0%	10901330
Alzheimer's	DDE	1.66 ng/mg cholesterol	6%	3.4	12.6%	24473795
ALS	Lead	2.38 ug/dL blood	33%	1.81	21.0%	25479292
ALS	DDT	Any exposure	>95% below LOD	2.1	Unknown at this time	PMC3358481
Brain CA	Lead	0.005 ug/dL	14%	1.9	~50.0%	17164378
Emotional disturbance in boys 3-5	BPA	8.50 ug/L	7%	1.62	2.7%	22543054

In-Process Example – Alzheimer's Dz

How to Interpret

No association	No apparent disease association
#.#	Disease risk (not yet converted to %)
%	% of Disease due to toxin
NAD	No available data
Insufficient data	Inadequate or contradictory data
Theoretical	Known mechanism but no research
??	Data very dirty
Blank	Research not yet reviewed

Alzheimer's Disease

Aluminum	3-33% (Dirty data!)
Arsenic	Theoretical
Benzene	NAD
Bisphenol A	Theoretical
Cadmium	Insufficient data
DDT/DDE	12%
Dioxins	Theoretical
Fluoride	Annecdotal - dentistry
Glyphosate	Theoretical
Lead	Insufficient data
Mercury	Insufficient data
Organochlorine pesticides	Theoretical
Organophosphate pesticides	2.0
Phthalates	Possible correlation, insuf. data
Polybrominated diphenyl ethers	NAD
Polycyclic aromatic hydrocarbons	NAD
PCBs	Insufficient data

Applying Same AF Formula to AD for "Conventional" Risk Factors

RISK FACTOR	POPULATION PREVALENCE	RELATIVE RISK (95% CI)	PAR% (Confidence Range)
Physical inactivity	32.5%	1.82 (1.19, 2.78)	21.0% (5.8%, 36.6%)
Depression	19.2%	1.90 (1.55, 2.33)	14.7% (9.6%, 20.3%)
Smoking	20.6%	1.59 (1.15, 2.20)	10.8% (3.0%, 19.8%)
Mid-life hypertension	14.3%	1.61 (1.16, 2.24)	8.0% (2.2%, 15.1%)
Mid-life obesity	13.1%	1.60 (1.34, 1.92)	7.3% (4.3%, 10.8%)
Low education	13.3%	1.59 (1.35, 1.86)	7.3% (4.4%, 10.3%)
Diabetes	8.7%	1.39 (1.17, 1.66)	3.3% (1.5%, 5.4%)
Combined			30.8% - 54.1%

Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. Lancet Neurol. 2011 Sep;10(9):819-28.

Portion of Population with Toxin Load Which Doubles Disease Risk

Toxin	Disease	% with Doubled Risk
Polycyclic aromatic hydrocarbons	Asthma	94%
PCB187	Breast Cancer	60%
Phthalates	Diabetes	55%
Lead	**ALS**	**33%**
Aluminum	**Alzheimer's Disease**	**25%**
DDT	**ADHD**	**25%**
PCBs	Diabetes	25%
Dioxin-like PCBs	Rheumatoid Arthritis	25%
Arsenic	Gout	23%
Bisphenol A	Diabetes	22%
Cigarette smoking	**Lung Cancer**	**21%**
Arsenic	Diabetes	20%
Polycyclic aromatic hydrocarbons	Diabetes	20%

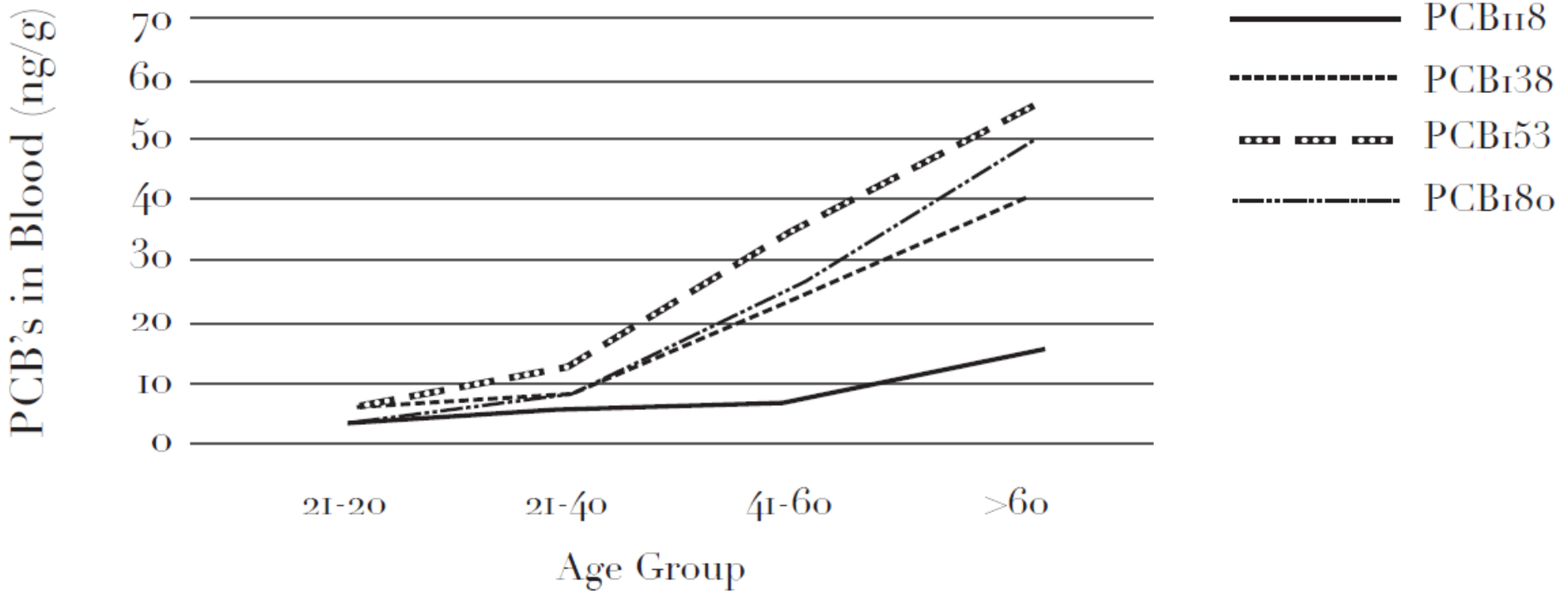
BIOACCUMULATION AND MECHANISMS OF DAMAGE

Toxin Half Lives in Blood and Tissues

Toxin	"Normal" (mg/L)	Acute Toxic (mg/L)	Half-Life
Arsenic	0.002-0.07	0.05-0.25	2-4 days (CDC)
Benzene	0.0002	60ppm	0.5-1.0 days
Cadmium	0.0003-0.0065	0.015-0.05	**16 years**
Chlordane	0.001	0.0025	3-4 days
DDT/DDE	Absent	285mg/kg	**2-10 years**
Dieldrin	0.0015	0.15-0.30	**2-12 months**
Ethanol	Absent	1000-2000	15%/hour
Lead	0.09	0.4-0.6	1-1.5 mo (2+ yrs bone)
Mercury	0.0015-0.002	0.05-0.2	**2 months (CDC)**
PCBs	<700ng/g lipid	700-1000ng/g lipid	**3-25 years!**
Toluene (hippuric acid)	1.5-1.6g/g creatinine	2.5g/g creatinine	0.5-3 days

Schulz M, et al. Therapeutic and toxic blood concentrations of nearly 1,000 drugs and other xenobiotics. Crit Care. 2012 Jul 26;16(4):R136

Bioaccumulation of Neurotoxins



DDT banned in 1972 PCBs banned in 1977

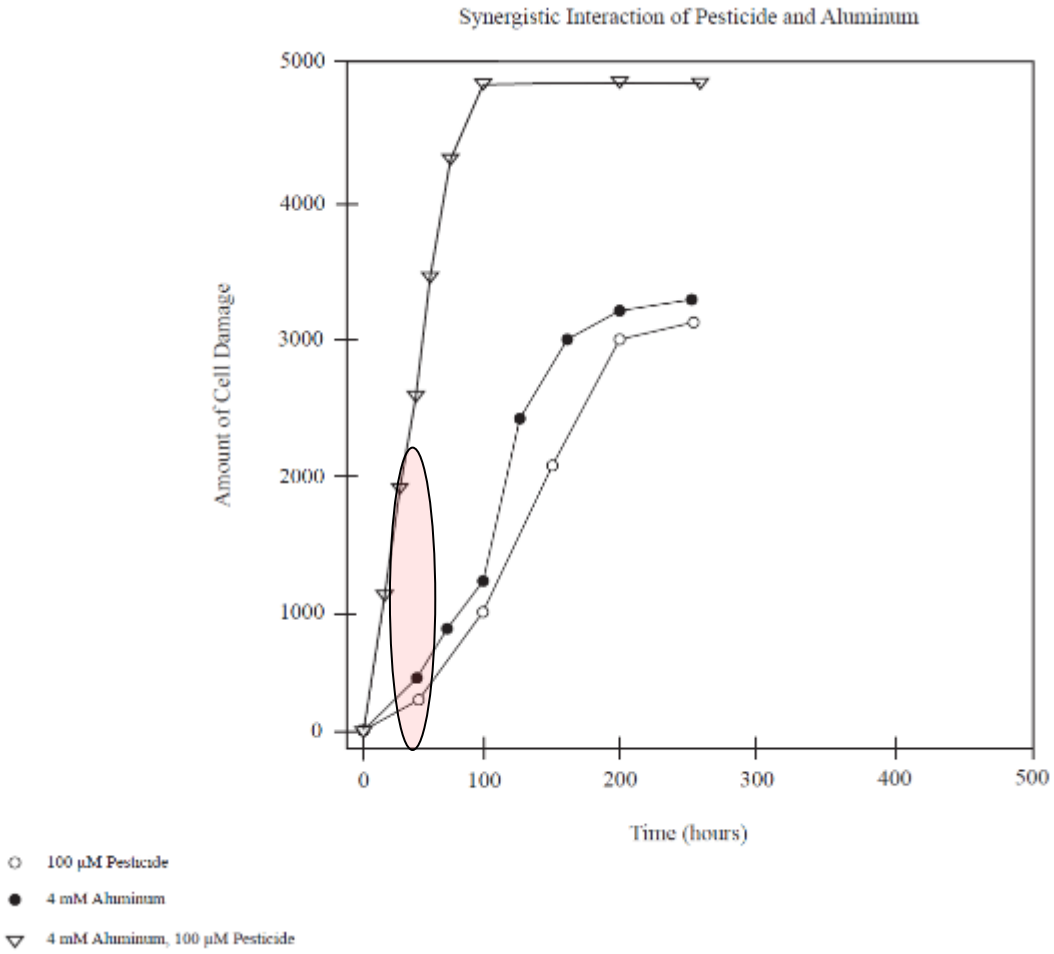
Serdar B, et al. Potential effects of polychlorinated biphenyls (PCBs) and selected organochlorine pesticides (OCPs) on immune cells and blood biochemistry measures: a cross-sectional assessment of the NHANES 2003-2004 data. *Environ Health*. 2014;13:114.

Neurotoxin Synergy

- Neuron cell study
- Damage (units):
  - 400 (OCP)

    +
  - 600 (AL)

    =
  - **2,000**



Uversky VN. Synergistic effects of pesticides and metals on the fibrillation of alpha-synuclein: implications for Parkinson's disease. Neurotoxicology. 2002;Oct;23(4-5):527-36.

Which are the Worst Toxins?

- According to the CDC
  - Toxicity
  - Population toxic load
  - Prevalence in toxic waste sites
- According to clinical importance (our research)
  - Exposure
  - % of disease
  - Ability of the body to detoxify/excrete

Agency for Toxic Substances and Disease Registry Priority List

2013 RANK	SUBSTANCE NAME	TOTAL POINTS	2011 RANK	CAS RN
1	ARSENIC	1670.4	1	007440-38-2
2	LEAD	1529.2	2	007439-92-1
3	MERCURY	1458.6	3	007439-97-6
4	VINYL CHLORIDE	1359.8	4	000075-01-4
5	POLYCHLORINATED BIPHENYLS	1343.5	5	001336-36-3
6	BENZENE	1328.5	6	000071-43-2
7	CADMIUM	1318.7	7	007440-43-9
8	BENZO(A)PYRENE	1304.7	8	000050-32-8
9	POLYCYCLIC AROMATIC HYDROCARBONS	1279.7	9	130498-29-2
10	BENZO(B)FLUORANTHENE	1251.2	10	000205-99-2
11	CHLOROFORM	1203.5	11	000067-66-3
12	AROCLOR 1260	1190.3	12	011096-82-5
13	DDT, P,P'-	1181.5	13	000050-29-3
14	AROCLOR 1254	1171.2	14	011097-69-1
15	DIBENZO(A,H)ANTHRACENE	1155.4	15	000053-70-3
16	TRICHLOROETHYLENE	1151.4	16	000079-01-6
17	CHROMIUM, HEXAVALENT	1146.9	17	018540-29-9
18	DIELDRIN	1142.5	18	000060-57-1
19	PHOSPHORUS, WHITE	1141.4	19	007723-14-0
20	HEXACHLOROBUTADIENE	1128.2	20	000087-68-3
21	DDE, P,P'-	1126.2	21	000072-55-9
22	CHLORDANE	1125.9	22	000057-74-9
23	COAL TAR CREOSOTE	1124.5	23	008001-58-9

The Worst Toxins Clinically

My Rank	Toxin	Diseases	Primary Sources
1	Arsenic	Cancers, diabetes, gout	Water, chicken, rice
2	DDT	**ADHD**, **dementia**, diabetes	Everywhere
3	Phthalates	**ADHD**, diabetes	Soft plastics, HABAs
4	PBDEs	**ADHD**, diabetes	Flame retardant fabrics
5	PAHs	**ADHD**, cancers, dyslipidemia	Smoking, charbroiling
6	PCBs	Cancers, diabetes, MI, RA	Everywhere
7	Mercury	**Dementia**	“Silver” fillings, fish
8	Lead	Cardiovascular disease, **IQ**	Paint, water
?	Glyphosate	Pending	Research invalid

ASSESSMENT

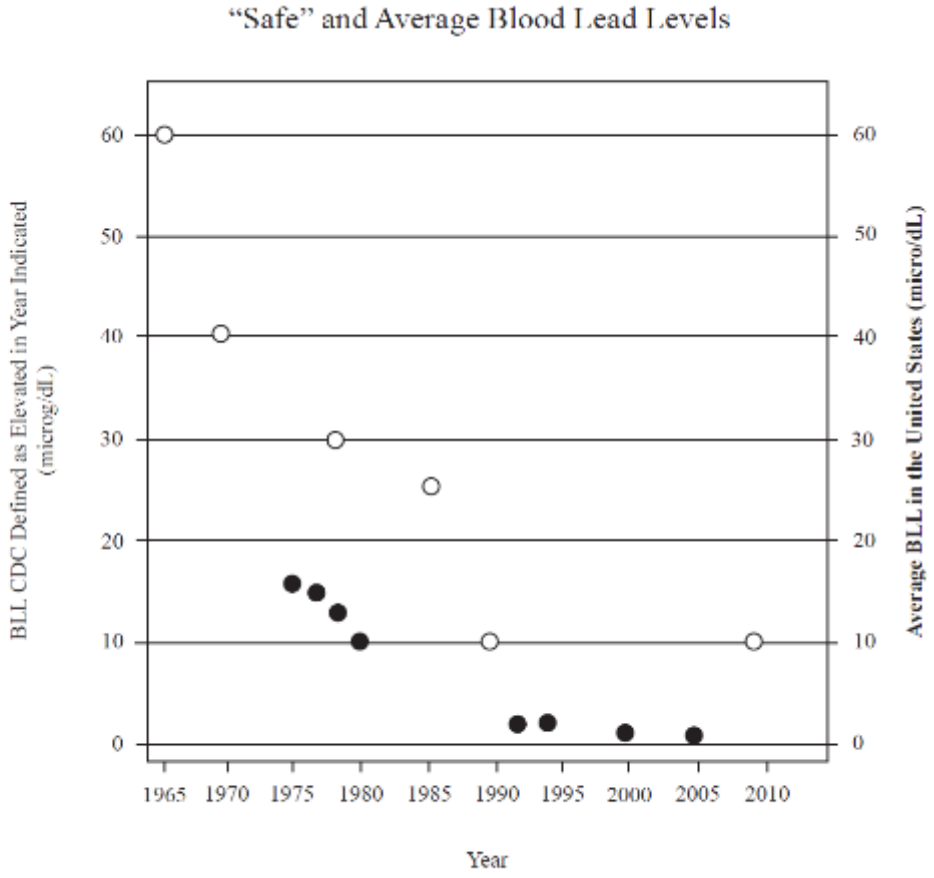
Assessment

- Direct measurement
- Body load/Historic exposure
  - Challenge testing
  - Toenails
  - Hair
- Indirect measures
  - GGTP
  - 8-OHdG
  - Conventional laboratory tests

Direct Assessment

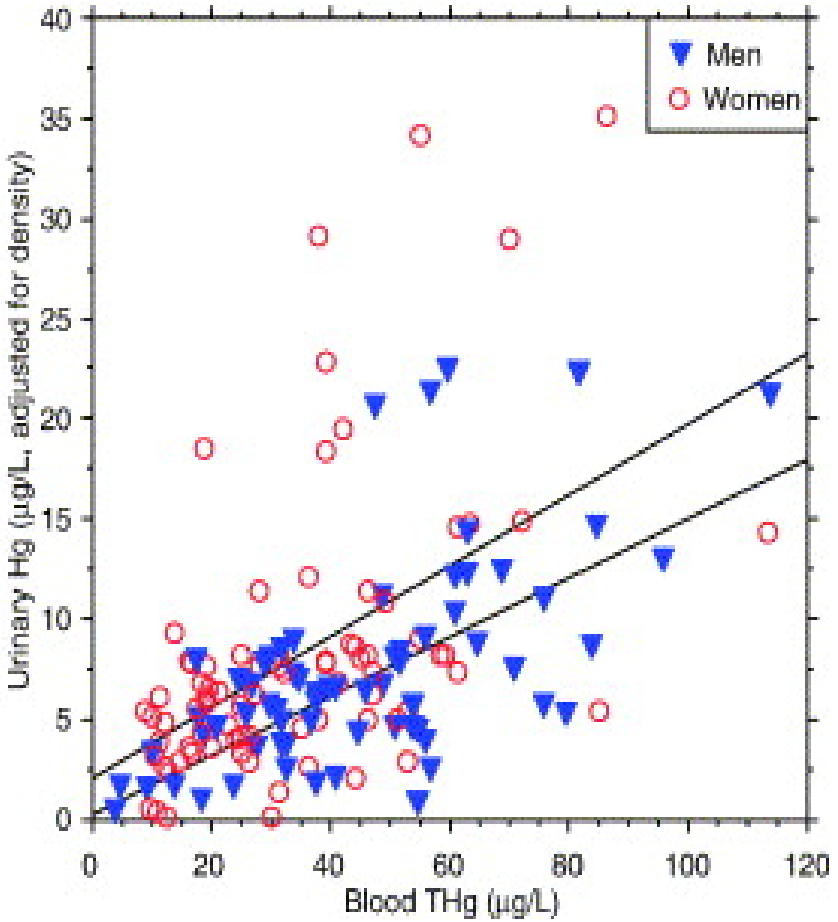
- Toxic metals:
  - Urine or blood levels considered the gold standard
    - Primarily indicate current exposure
    - Poor intercorrelations
    - Correlation with body load controversial
    - 95% standard questionable
- Persistent organic pollutants and solvents
  - Direct measure in blood and urine now available
  - Fat biopsy measurement more indicative of body load
    - Invasive and expensive

“Safe” Lead Levels 6-Fold Lower Than Original 1965 95% Standard



Poor Hg Inter-Test Correlation

- **Poor correlation between blood and urine** , r = 0.30
- Better correlation between blood and hair, r = 0.56



Zimmera H, et al. Determination of mercury in blood, urine and saliva for the biological monitoring of an exposure from amalgam fillings in a group with self-reported adverse health effects. Int. J. Hyg. Environ. Health 2002;205(3):205-211

Berglund M, et al. Inter-individual variations of human mercury exposure biomarkers: a cross-sectional assessment. Environ Health. 2005 Oct 3;4:20

Pre-Urine

TOXIC METALS		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	< dl	< 25	
Antimony	(Sb)	< dl	< 0.2	
Arsenic	(As)	39	< 75	
Barium	(Ba)	0.5	< 7	
Beryllium	(Be)	< dl	< 1	
Bismuth	(Bi)	< dl	< 2	
Cadmium	(Cd)	0.4	< 0.8	
Cesium	(Cs)	5.3	< 9	
Gadolinium	(Gd)	< dl	< 0.5	
Lead	(Pb)	0.1	< 2	
Mercury	(Hg)	2.4	< 3	
Nickel	(Ni)	1.1	< 8	
Palladium	(Pd)	< dl	< 0.1	
Platinum	(Pt)	< dl	< 0.1	
Tellurium	(Te)	< dl	< 0.5	
Thallium	(Tl)	0.4	< 0.5	
Thorium	(Th)	< dl	< 0.03	
Tin	(Sn)	0.4	< 4	
Tungsten	(W)	< dl	< 0.4	
Uranium	(U)	< dl	< 0.03	

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	178	35- 240	

SPECIMEN DATA

Comments:

Date Collected: 01/09/2017
Date Received: 01/11/2017
Date Completed: 01/12/2017

pH upon receipt: **Acceptable**
<dl: less than detection limit
Provoking Agent:

Collection Period: **Random**
Volume:
Provocation: **PRE PROVOCATIVE**

Post-Urine

DMPS: 300mg
DMSA: 500 mg
Urine collected
6 hours

Toxic Metals; Urine

TOXIC METALS		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	5.2	< 25	
Antimony	(Sb)	0.2	< 0.2	
Arsenic	(As)	140	< 75	
Barium	(Ba)	0.8	< 7	
Beryllium	(Be)	< dl	< 1	
Bismuth	(Bi)	0.3	< 2	
Cadmium	(Cd)	0.4	< 0.8	
Cesium	(Cs)	6.3	< 9	
Gadolinium	(Gd)	< dl	< 0.5	
Lead	(Pb)	6.9	< 2	
Mercury	(Hg)	53	< 3	
Nickel	(Ni)	1.7	< 8	
Palladium	(Pd)	< dl	< 0.1	
Platinum	(Pt)	< dl	< 0.1	
Tellurium	(Te)	< dl	< 0.5	
Thallium	(Tl)	0.5	< 0.5	
Thorium	(Th)	< dl	< 0.03	
Tin	(Sn)	14	< 4	
Tungsten	(W)	< dl	< 0.4	
Uranium	(U)	< dl	< 0.03	

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	82.5	35- 240	

SPECIMEN DATA

Comments:

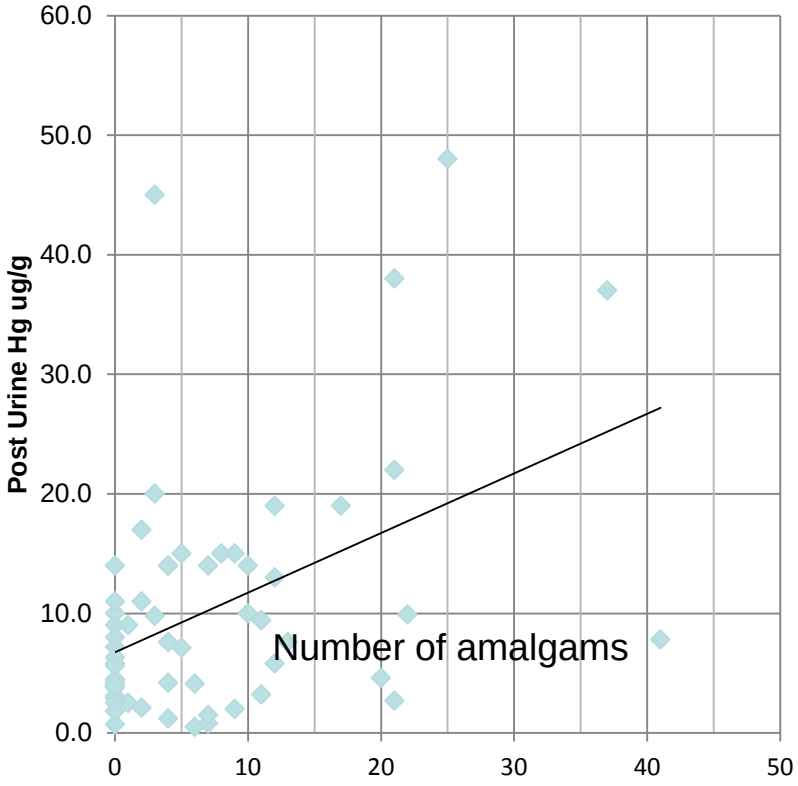
Date Collected: 01/09/2017
Date Received: 01/12/2017
Date Completed: 01/13/2017

pH upon receipt: Acceptable
<dl: less than detection limit
Provoking Agent: DMSA 500MG, DMPS

Collection Period: Random
Volume:
Provocation: POST PROVOCATIVE

Hg Assessment Correlations

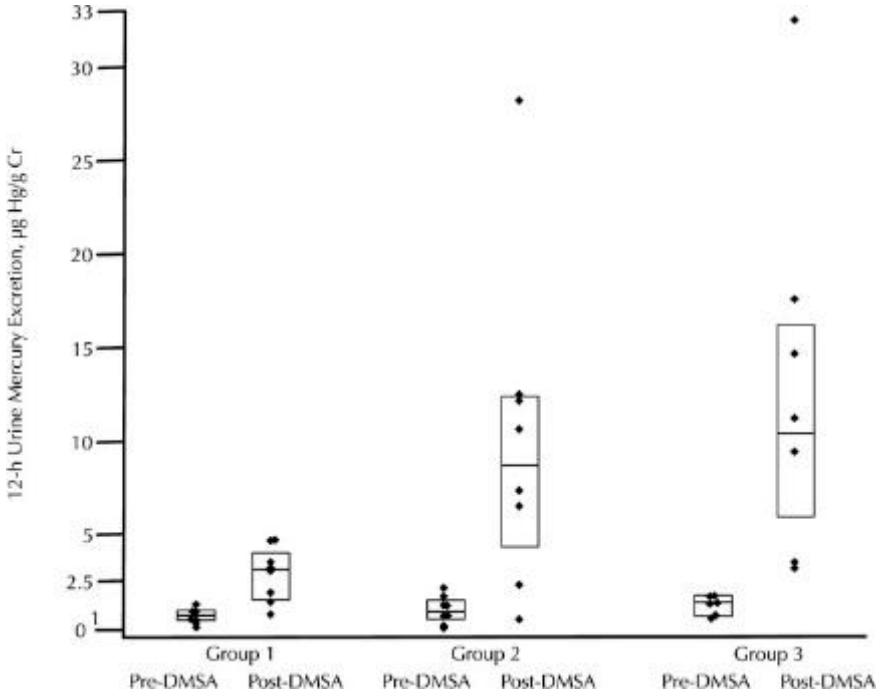
- Extensive measurements in 65
  - Whole blood Hg
  - Oral DMPS challenge
  - Amalgam surfaces
- Correlations
  - Whole blood w pre urine: r = 0.40
  - Whole blood w post urine: r = 0.57
  - Pre urine w post urine: r = 0.68
  - Amalgams w pre urine: r = 0.26
  - Amalgams w whole blood: r = 0.36
  - **Amalgams with post urine: 0.44**
- Preliminary support that challenge testing is better



Pizzorno J, Markin A. Unpublished research. 2010

Challenge Testing: Correlates with Fish Consumption

- Compared 0 to 1-2 to 3 or more servings per week
- First urine showed essentially no differentiation
- Challenge testing showed clear correlation
- Still a lot of variation

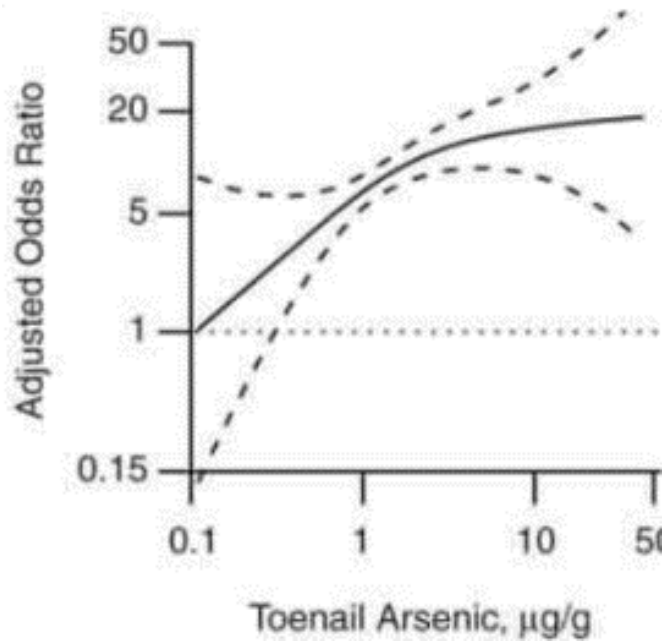


Ruha AM, et al. Urine mercury excretion following meso-dimercaptosuccinic acid challenge in fish eaters. Arch Pathol Lab Med. 2009;133(1):87-92.

Historic: Toenail Arsenic Correlates with Diabetes

How As causes diabetes

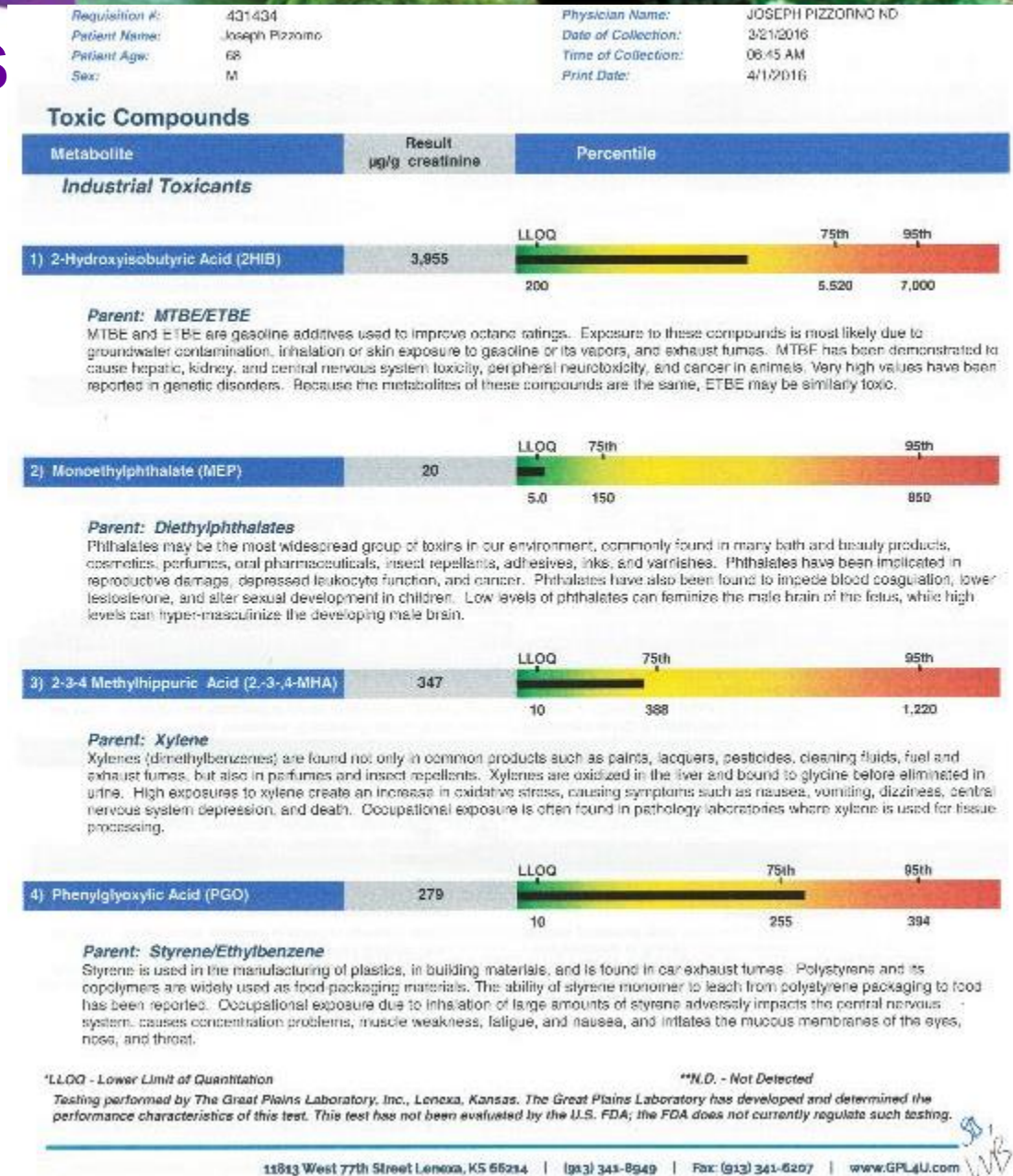
- Blocks sugar stimulating insulin secretion
- Epigenetic inhibition of sugar regulation



Pan W-C, Seow WJ, Kile ML, et al. Association of low to moderate levels of arsenic exposure with risk of Type 2 diabetes in Bangladesh. American Journal of Epidemiology. 2013;178(10):1563-70

Direct: Chemicals

- Measuring chemicals and POP load directly
  - Urine sample
  - 150+ environmental chemicals



Requisition #:	431434	Physician Name:	JOSEPH PIZZORNO ND
Patient Name:	Joseph Pizzorno	Date of Collection:	3/21/2016
Patient Age:	68	Time of Collection:	08:45 AM
Sex:	M	Print Date:	4/1/2016

Toxic Compounds

Metabolite	Result µg/g creatinine	Percentile
Industrial Toxicants		
1) 2-Hydroxyisobutyric Acid (2HIB)	3,955	LLOQ 200 · 75th 5,520 · 95th 7,000

Parent: MTBE/ETBE

MTBE and ETBE are gasoline additives used to improve octane ratings. Exposure to these compounds is most likely due to groundwater contamination, inhalation or skin exposure to gasoline or its vapors, and exhaust fumes. MTBE has been demonstrated to cause hepatic, kidney, and central nervous system toxicity, peripheral neurotoxicity, and cancer in animals. Very high values have been reported in genetic disorders. Because the metabolites of these compounds are the same, ETBE may be similarly toxic.

2) Monoethylphthalate (MEP)	20	LLOQ 5.0 · 75th 150 · 95th 850

Parent: Diethylphthalates

Phthalates may be the most widespread group of toxins in our environment, commonly found in many bath and beauty products, cosmetics, perfumes, oral pharmaceuticals, insect repellents, adhesives, inks, and varnishes. Phthalates have been implicated in reproductive damage, depressed leukocyte function, and cancer. Phthalates have also been found to impede blood coagulation, lower testosterone, and alter sexual development in children. Low levels of phthalates can feminize the male brain of the fetus, while high levels can hyper-masculinize the developing male brain.

3) 2-3-4 Methylhippuric Acid (2,-3-,4-MHA)	347	LLOQ 10 · 75th 388 · 95th 1,220

Parent: Xylene

Xylenes (dimethylbenzenes) are found not only in common products such as paints, lacquers, pesticides, cleaning fluids, fuel and exhaust fumes, but also in perfumes and insect repellents. Xylenes are oxidized in the liver and bound to glycine before eliminated in urine. High exposures to xylene create an increase in oxidative stress, causing symptoms such as nausea, vomiting, dizziness, central nervous system depression, and death. Occupational exposure is often found in pathology laboratories where xylene is used for tissue processing.

4) Phenylglyoxylic Acid (PGO)	279	LLOQ 10 · 75th 255 · 95th 394

Parent: Styrene/Ethylbenzene

Styrene is used in the manufacturing of plastics, in building materials, and is found in car exhaust fumes. Polystyrene and its copolymers are widely used as food packaging materials. The ability of styrene monomer to leach from polystyrene packaging to food has been reported. Occupational exposure due to inhalation of large amounts of styrene adversely impacts the central nervous system, causes concentration problems, muscle weakness, fatigue, and nausea, and irritates the mucous membranes of the eyes, nose, and throat.

*LLOQ - Lower Limit of Quantitation **N.D. - Not Detected

Testing performed by The Great Plains Laboratory, Inc., Lenexa, Kansas. The Great Plains Laboratory has developed and determined the performance characteristics of this test. This test has not been evaluated by the U.S. FDA; the FDA does not currently regulate such testing.

11813 West 77th Street Lenexa, KS 66214 | (913) 341-8949 | Fax: (913) 341-6207 | www.GPL4U.com

Conventional Laboratory Tests Reflect Toxic Load in “Normal” Range

- Surprising number show toxin exposure
  - CBC: RBC, WBC, platelet count, hemoglobin, basophilic stippling
  - Liver enzymes: ALT, GGTP
  - Inflammatory markers: CRP
  - Lipids: LDL, oxLDL, triglycerides
  - Blood sugar: insulin, FBS, 2-hour PP
  - Metabolites: bilirubin, uric acid, homocysteine, 8-OHdG
  - Thyroid: T3, T4, TSH
- The historic “normal” range has been changing as the population has become more toxic

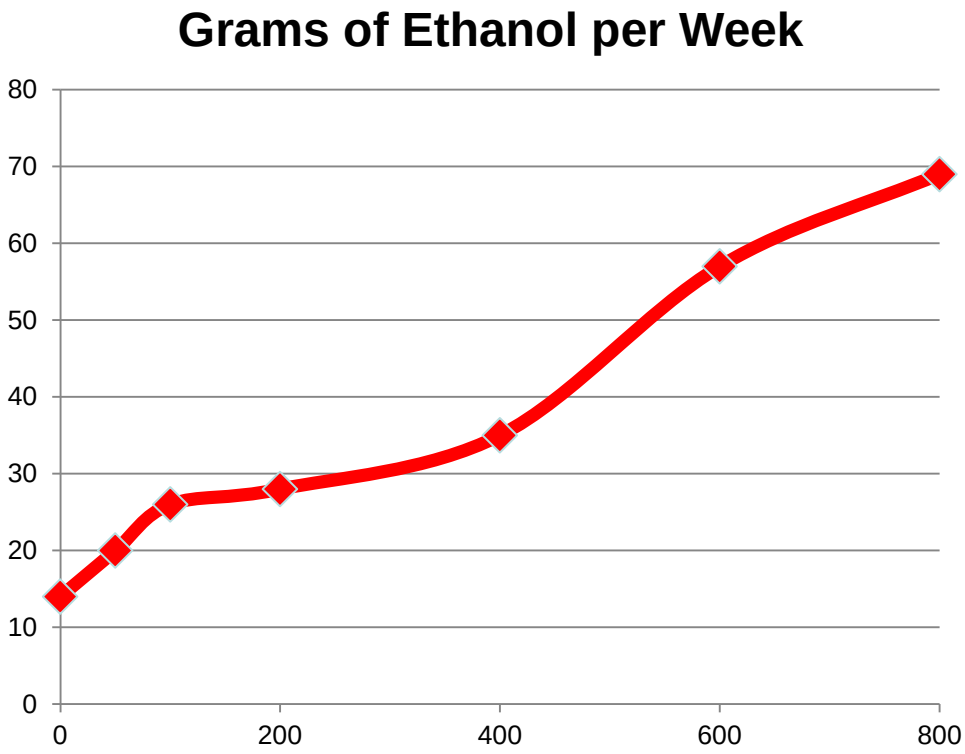
GGT: Indirect Measure of Toxin Load

- Exposure to POPs and metals induces GGTP as a defensive mechanism.
- **Within normal range** predicts:
  - All cause mortality
  - Type 2 diabetes
  - Coronary heart disease, hypertension, stroke, dyslipidemia,
  - Chronic kidney disease
  - Cancer.
- Cumulative biomarker for environmental pollutants.
- But not useful in the 10% with certain polymorphisms

Lee DH, et al (2003) Gamma-glutamyltransferase and diabetes—a 4 year follow-up study. Diabetologia 46:359–364
Lee DH, et al. Serum gamma-glutamyltransferase: new insights about an old enzyme. J Epidemiol Community Health. 2009 Nov;63(11):884-6.

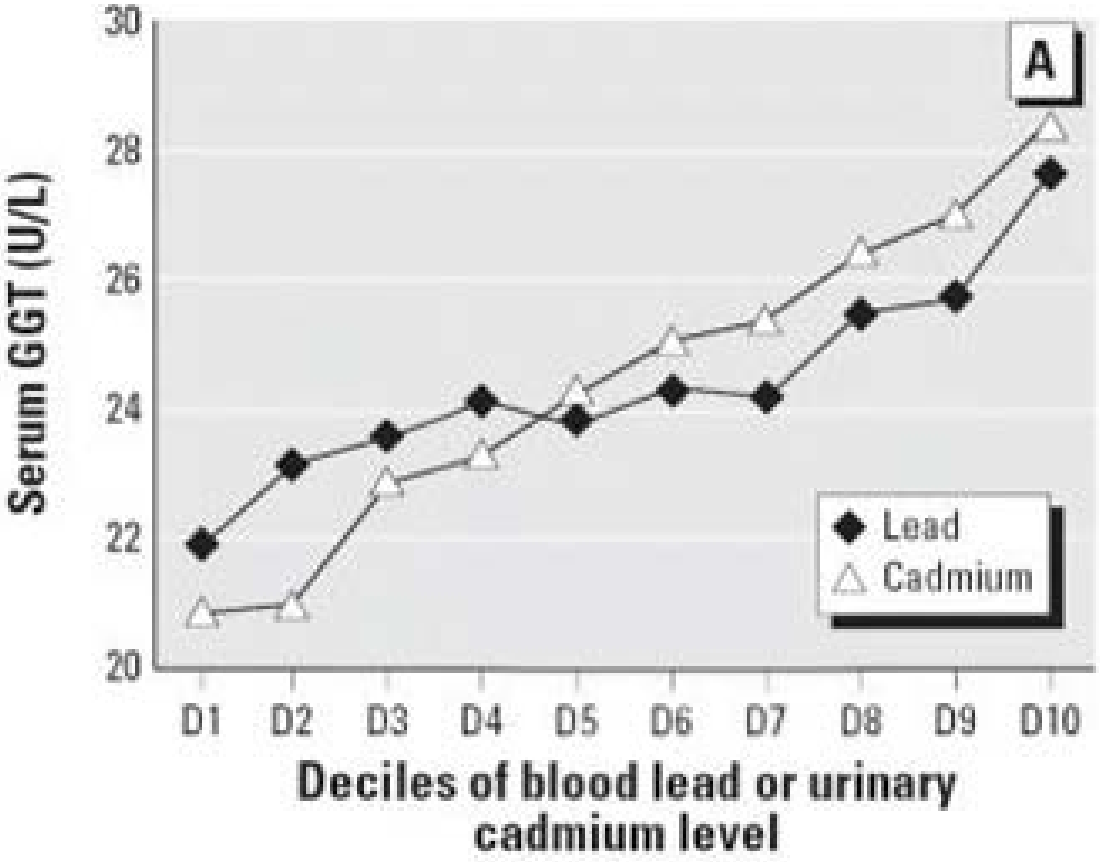
GGT and Alcohol Consumption

- **GGT directly correlates with alcohol consumption**
- 40 g/d elevates GGT ~15%
- **Watch for false negatives**
  - Genomic variation
  - Are these the ones most sensitive to/damaged by chemical toxins?
- Could up-regulation of GGT in light alcohol consumption be reason for benefit?



Adapted from: Nagaya T, et al. Dose-response relationships between drinking and serum tests in Japanese men aged 40–59 years. Alcohol 1999 Feb. 17(2): 133–8.

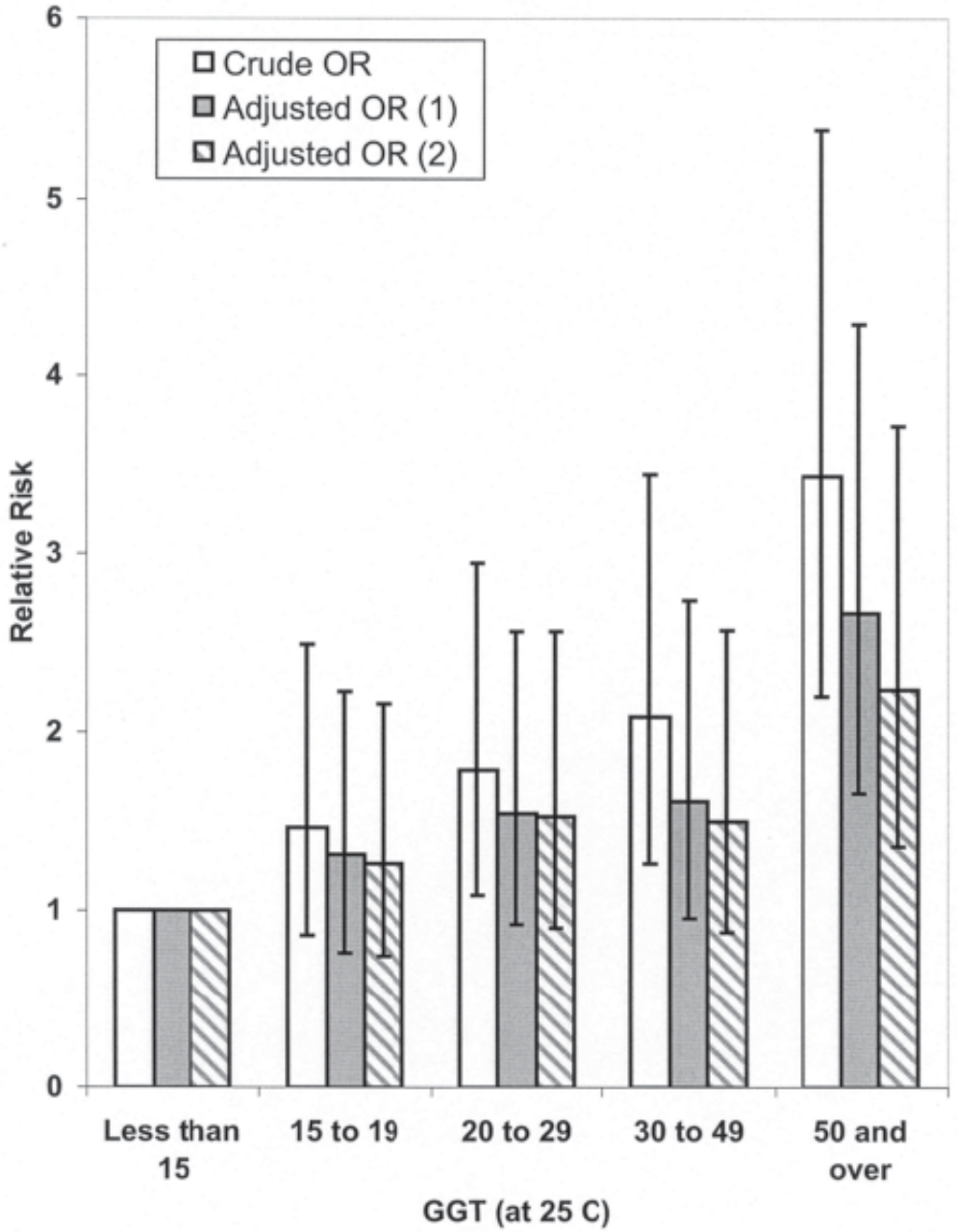
GGT Correlates With Toxic Metal Levels



Lee DH, et al. Graded associations of blood lead and urinary cadmium concentrations with oxidative-stress-related markers in the U.S. population: results from the third National Health and Nutrition Examination Survey. Environ Health perspect. 2006 Mar;114(3):350-4

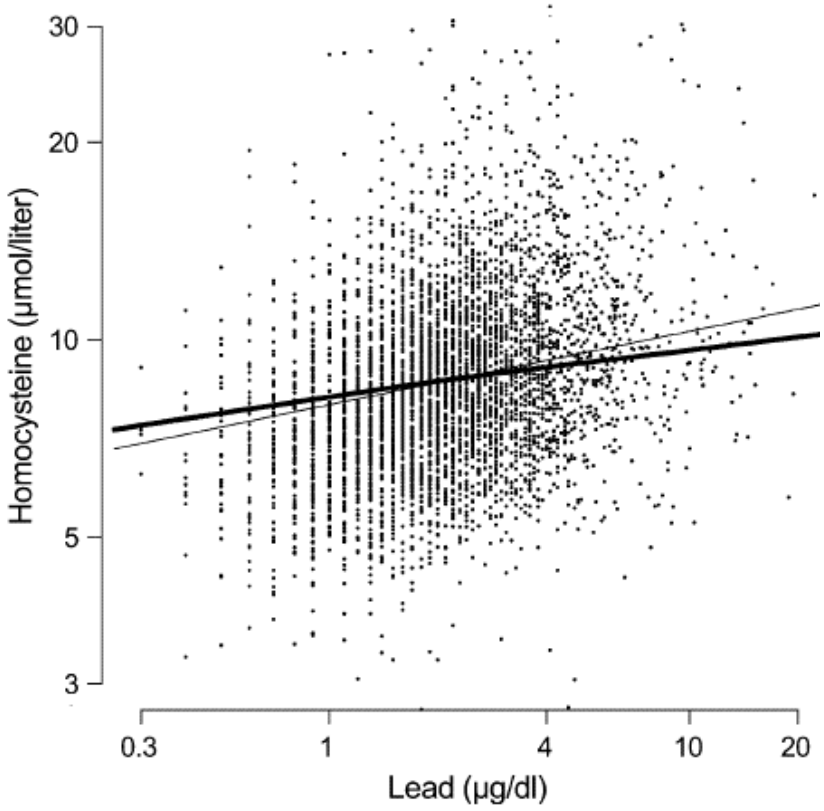
GGT Levels Correlate with Risk of Death

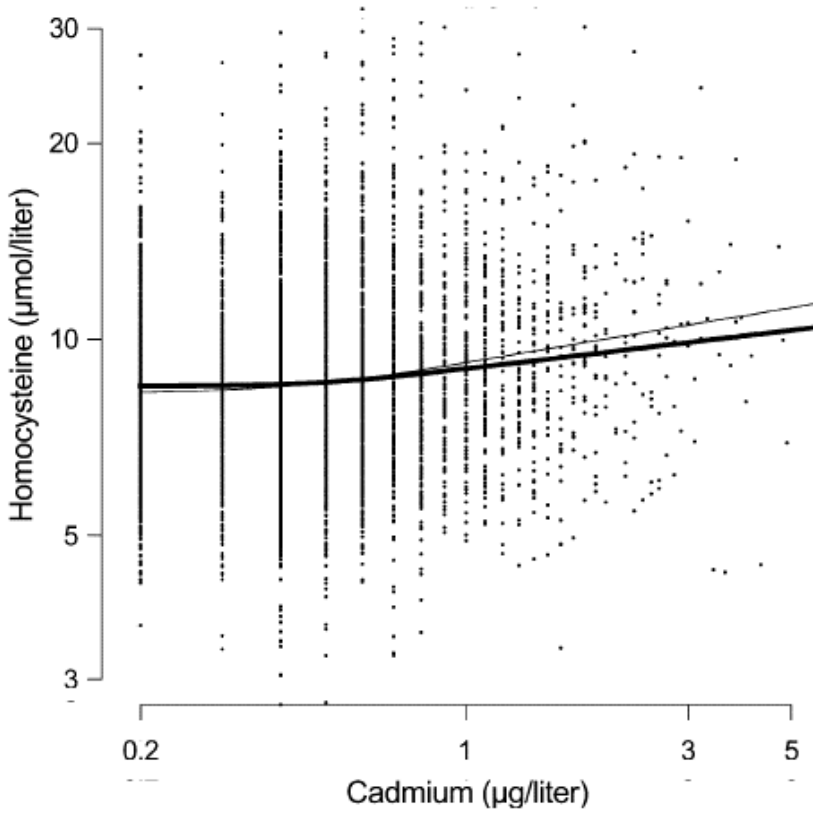
- **GGT over 50 associated with tripling of death rate!**
- 30-40 associated with doubling



Brenner H, et al. Distribution, determinants, and prognostic value of GGT for all-cause mortality in a cohort of construction workers from southern Germany. Prev Med 1997; 26: 305–10.

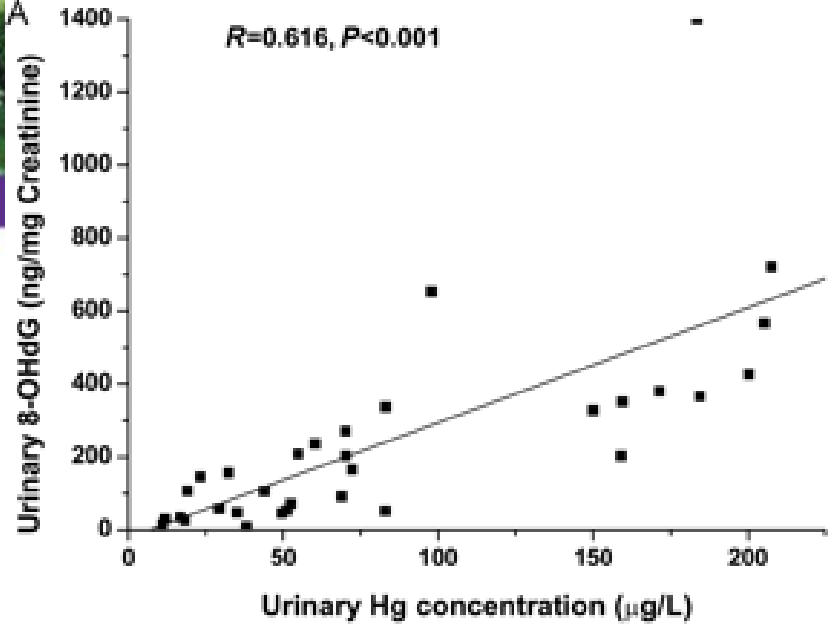
Homocysteine is Increased by Pb & Cd

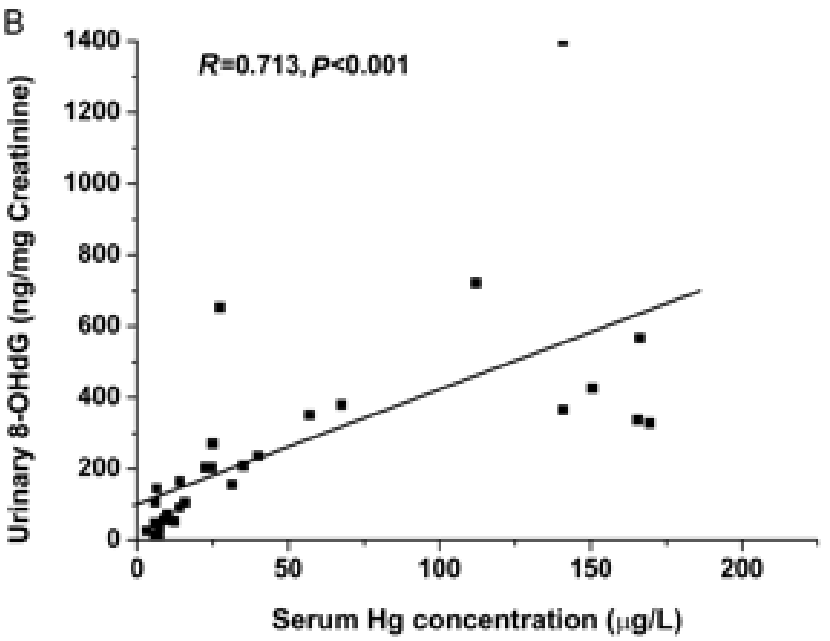




Guallar E, et al. Confounding of the relation between homocysteine and peripheral arterial disease by lead, cadmium, and renal function. Am J Epidemiol. 2006 Apr 15;163(8):700-8

8-OHdG Correlates with Mercury

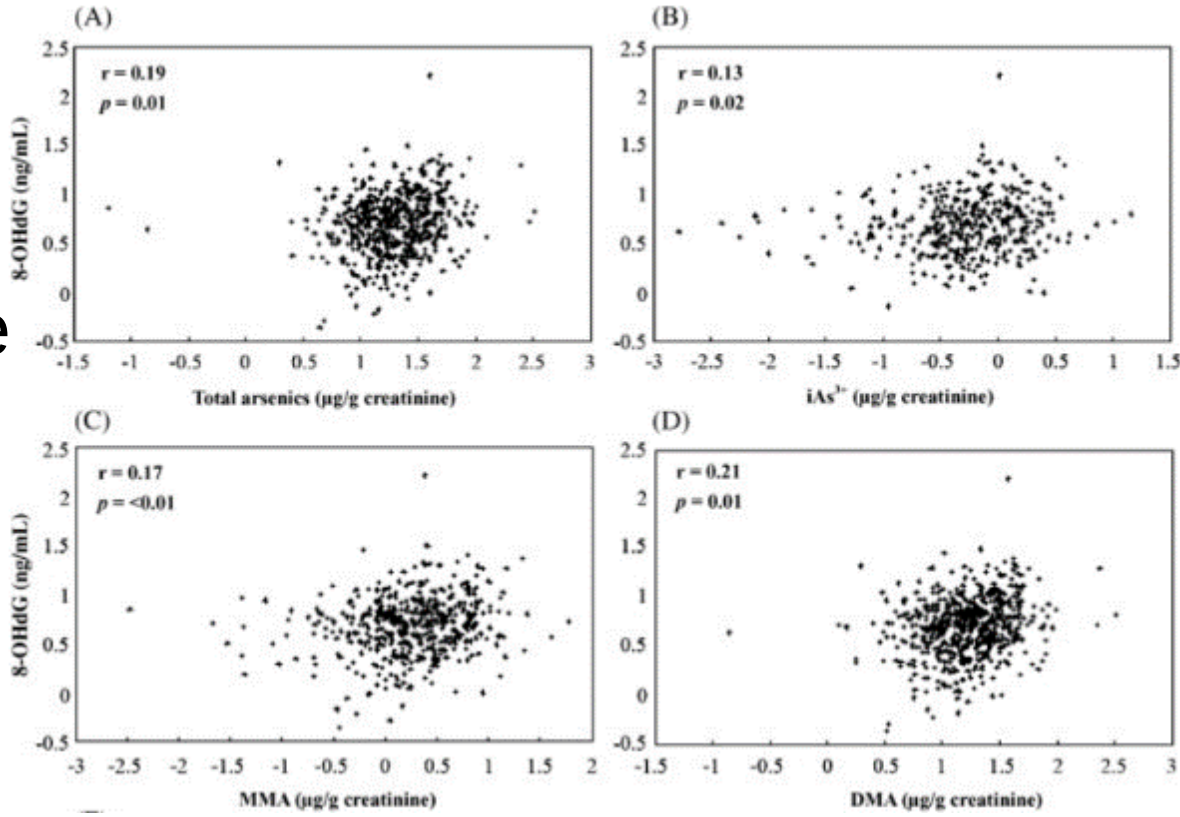




Chen C, et al. Increased oxidative DNA damage, as assessed by urinary 8-hydroxy-2'-deoxyguanosine concentrations, and serum redox status in persons exposed to mercury. Clin Chem. 2005 Apr;51(4):759-67

8-OHdG Correlates with Arsenic Load

- Urinary 8-OHdG measures DNA damage
- Many studies have found significant correlation with levels of typical forms of As



Chung CJ, Huang CJ, Pu YS, et al. Urinary 8-hydroxydeoxyguanosine and urothelial carcinoma risk in low arsenic exposure area. Toxicol Appl Pharmacol. 2008 Jan 1;226(1):14-21

INTERVENTION

Intervention

- Avoidance, AVIODANCE, **AVOIDANCE**
- Facilitate detoxification
- Increase excretion
- Supply competitive nutrients
- Decrease damage

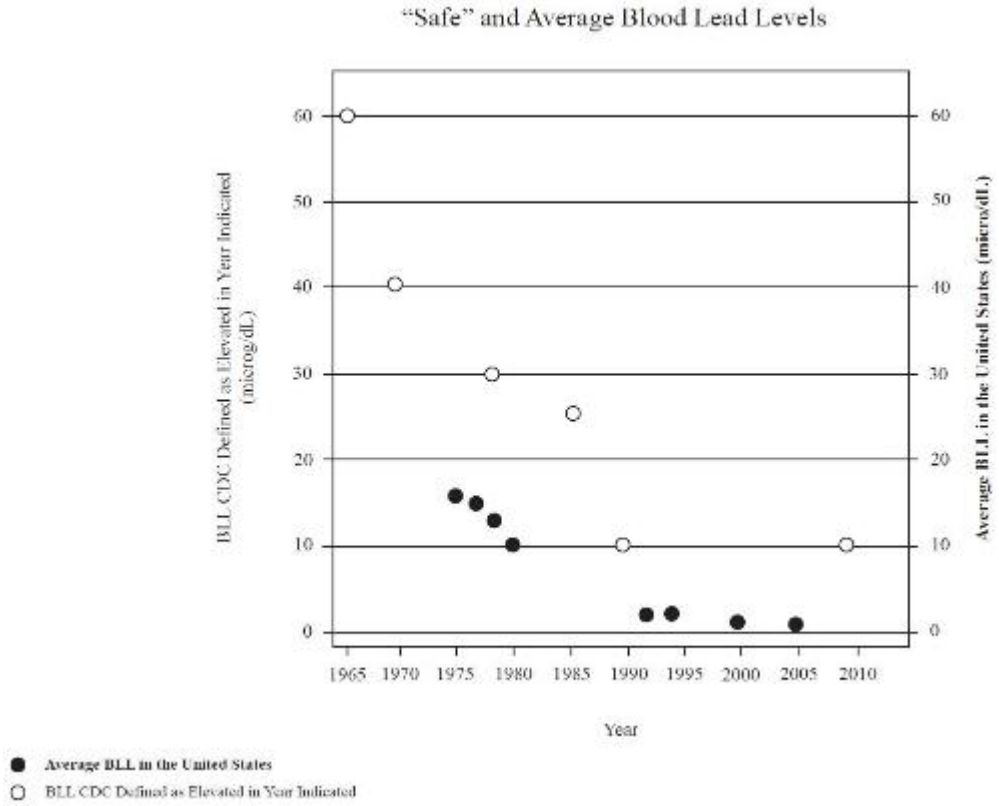
Sources of Toxins

- 60% Food
- 10% Water
- 10% House and yard chemicals
- 10% Health and beauty aids
- 5% Air

These are my best estimates, will likely change as new research becomes available

Public Health Can Decrease Toxic Load

- Banning lead in gasoline and paint worked—blood levels down dramatically.
- No threshold for safety –
  - **Children who had whole blood lead concentrations of <5 µg/dL (supposedly safe) associated with decreased IQ**
  - **2.4 million children at levels between 5 and 9.9 ug/dL**
- July 2012: CDC changed recommended level to intervene in children from 10 to 5.0 ug/dL. Eliminated term “level of concern”, to avoid false sense of safety.



Iqbal S, et al. Estimated burden of blood lead levels 5 microg/dl in 1999-2002 and declines from 1988 to 1994. Environ Res. 2008
http://www.cdc.gov/nceh/lead/acclpp/cdc_response_lead_exposure_recs.pdf
http://www.environment.ucla.edu/reportcard/article3772.html

Mercury In Fish

- 10-fold variation from lowest to highest
- All fish contain some mercury
- Pick those with highest omega-3 and lowest Hg:
  - Sardines
  - Anchovies
  - Small salmon

Guide to mercury levels in different varieties of fish and shellfish

LOW-MERCURY FISH AND SHELLFISH

VERY LOW	BELOW AVERAGE
Shrimp	Pollock
Sardines	Atlantic Mackerel
Tilapia	Anchovies, Herring & Shad
Oysters & Mussels	Flounder, Sole & Plaice
Clams	Crabs
Scallops	Pike
Salmon	Butterfish
Crayfish	Catfish
Freshwater Trout	Squid
Ocean Perch & Mullet	Atlantic Croaker
	Whitefish

MODERATE-MERCURY FISH AND SHELLFISH

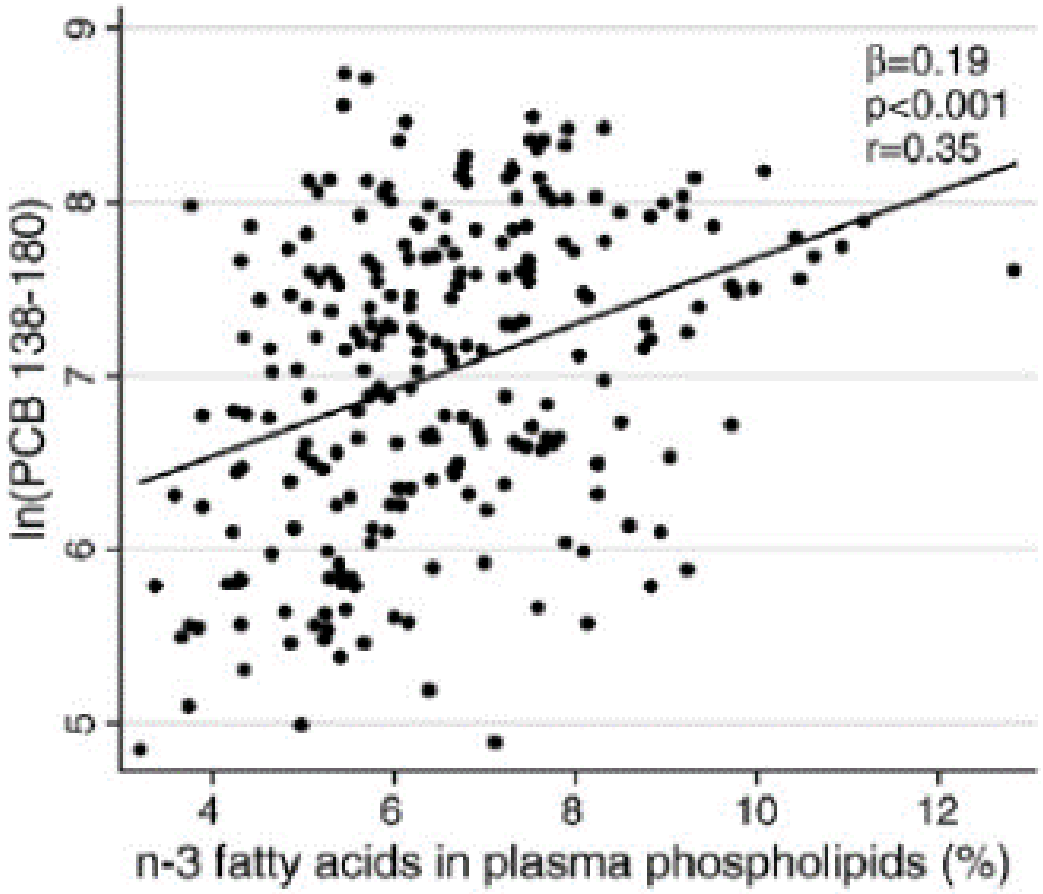
ABOVE AVERAGE	MODERATELY HIGH
Pacific Mackerel (Chub)	Carp & Buffalofish
Smelt	Halibut
Atlantic Tilefish	Sea Trout
Cod	Sablefish
Caned Light Tuna	Lingcod & Scorpionfish
Spiny Lobster	Sea Bass
Snapper, Porgy, Sheepshead	Pacific Croaker
Skate	American Lobster
Freshwater Perch	Freshwater Bass
Haddock, Hake, Monkfish	Bluefish

HIGH-MERCURY FISH

HIGH	VERY HIGH
Canned Albacore Tuna	King Mackerel
Spanish Mackerel	Swordfish
Fresh/Frozen Tuna	Shark
Grouper	Gulf Tilefish
Marlin	Tuna Sushi/Bluefin Tuna
Orange Roughy	

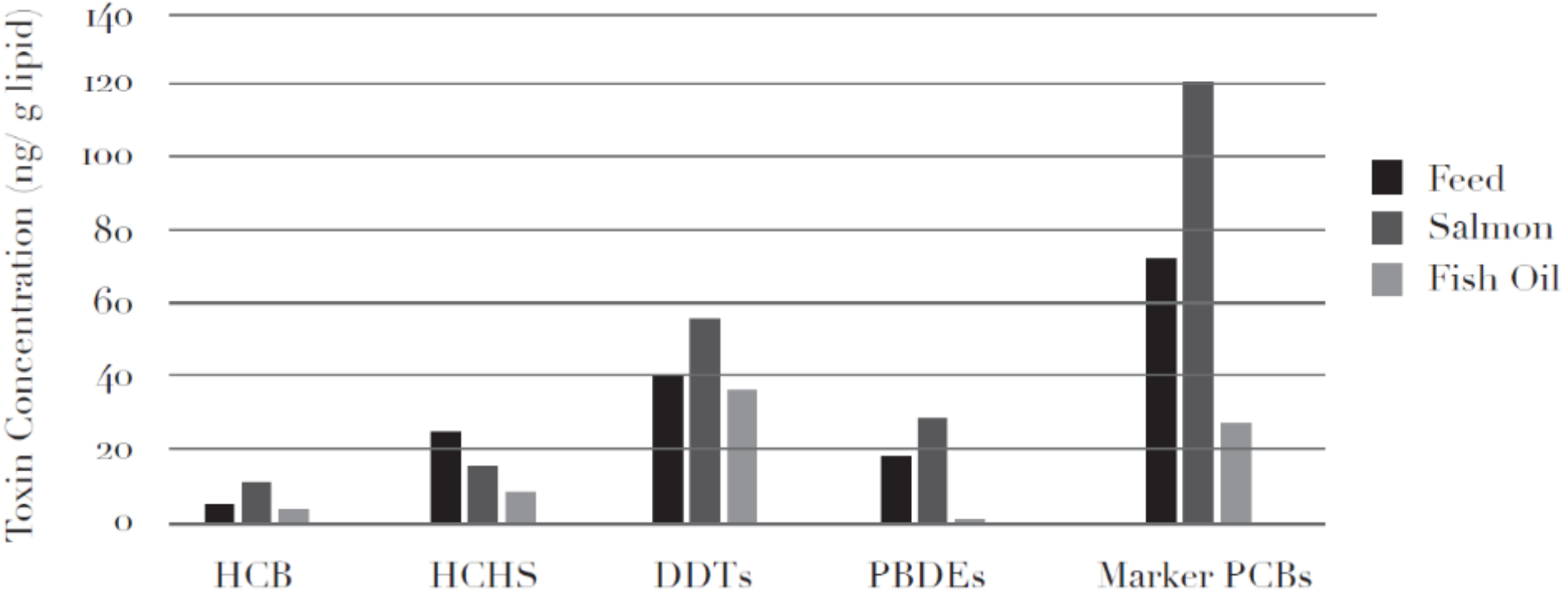
Source: http://www.fda.gov/Food/FoodSafety/Product-SpecificInformation/Seafood/FoodbornePathogensContaminants/Methylmercury/ucm115644.htm

Fish (esp farmed) a Significant Source of POPs



Bjermo H, et al. Fish intake and breastfeeding time are associated with serum concentrations of organochlorines in a Swedish population. Environ Int. 2013 Jan;51:88-96

PCBs in Farmed Fish



Jacobs MN, Covaci A, Schepens P. Investigation of selected persistent organic pollutants in farmed Atlantic salmon (Salmo salar), salmon aquaculture feed, and fish oil components of the feed. Environmental Science & Technology 2002;36: 2797–805

Worst/Best Foods (www.ewg.org 4/17)

Dirty Dozen™

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

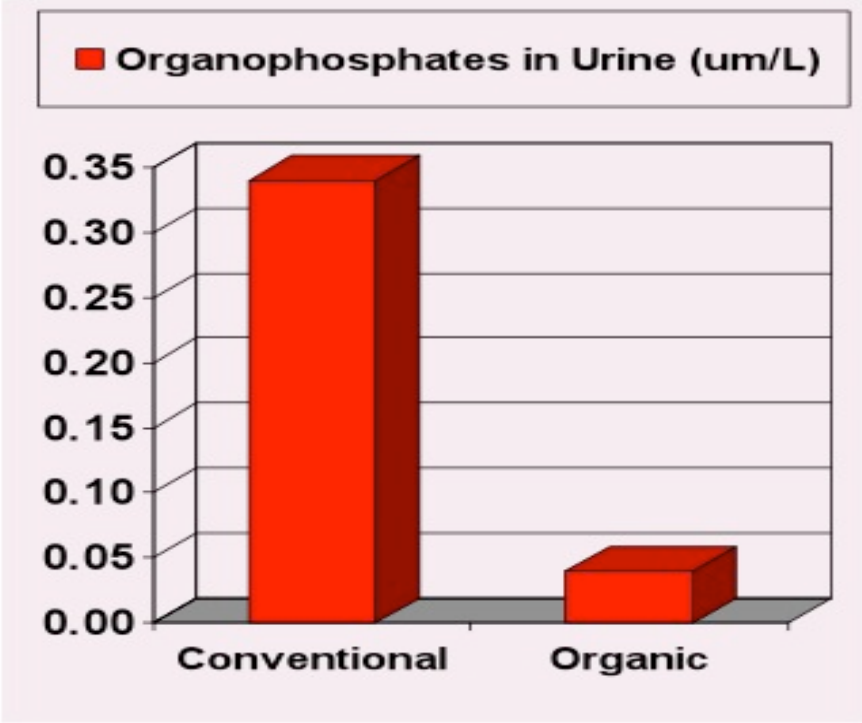
- Hot peppers
- Kale

Clean 15™

1. Sweet Corn
2. Avocado
3. Pineapples
4. Cabbage
5. Onions
6. Sweet Peas
7. Papayas
8. Asparagus
9. Mangoes
10. Eggplant
11. Honeydew melon
12. Kiwi Fruit
13. Cantaloupe
14. Cauliflower
15. Grapefruit

Eating Organically Grown Foods Dramatically Decreases Neurotoxins

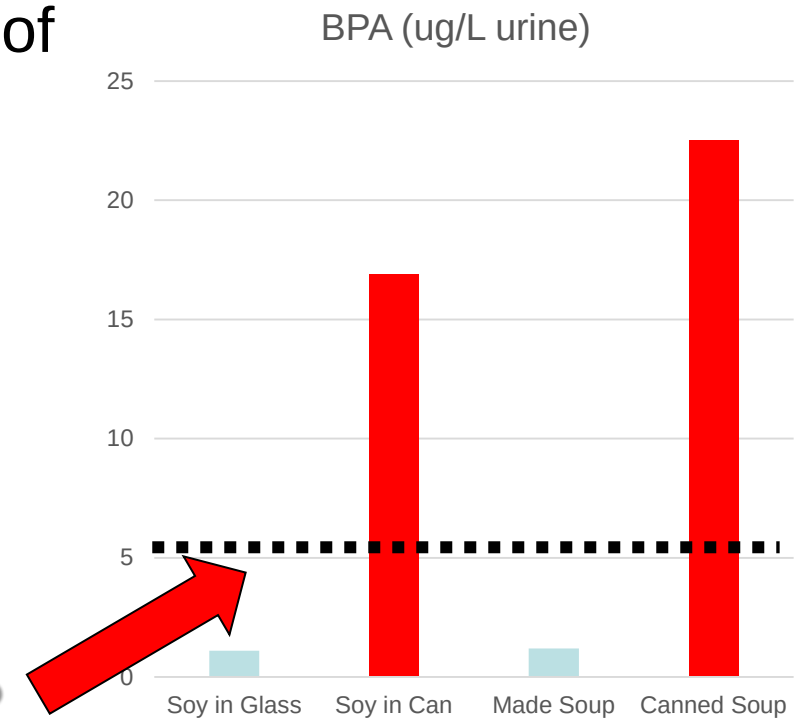
- Study done in Seattle children
- 10-fold increase in POPs doubles ADHD
- **Blood levels drop measurably within 3 days of eating only organically grown foods**



Curl CL, et al. Organophosphorus pesticide exposure of urban and suburban preschool children with organic and conventional diets. Env Health Perspect. 2003;111:377-82
Bouchard MF, et al. Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides. Pediatrics. 2010 Jun;125(6):e1270-7

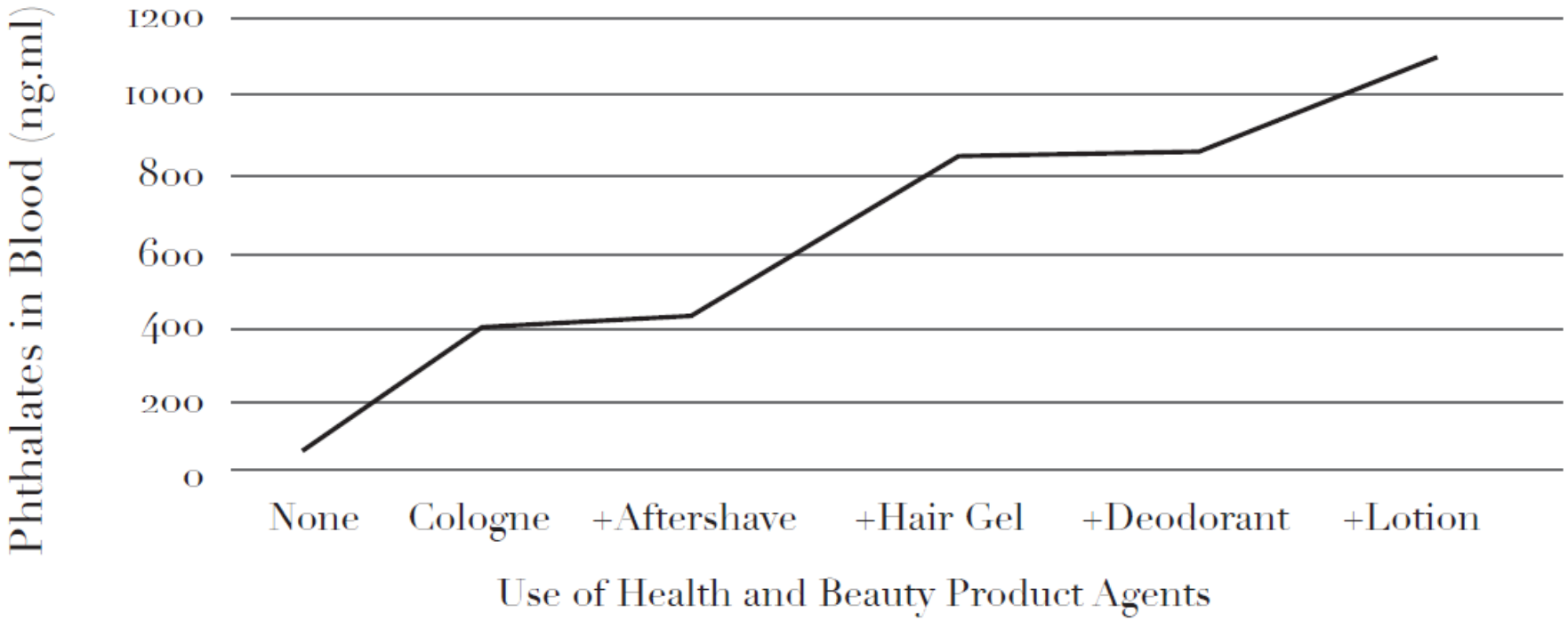
BPA: Home-Made or Glass Containers

- 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?**



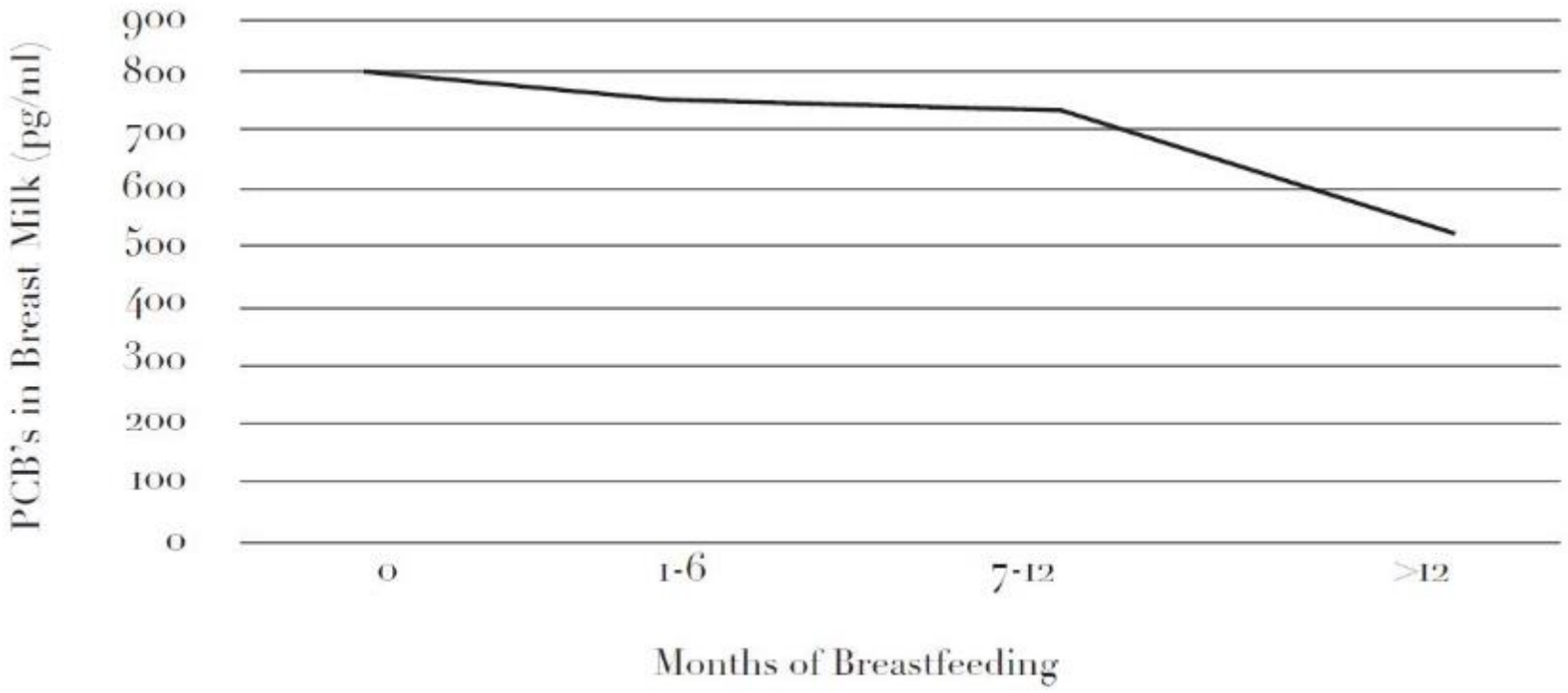
Carwile JL1, Ye X, Zhou X, et al. Canned soup consumption and urinary bisphenol A: a randomized crossover trial. JAMA. 2011 Nov 23;306(20):2218-20.
Bae S1, Hong YC2. Exposure to bisphenol A from drinking canned beverages increases blood pressure: randomized crossover trial. Hypertension. 2015 Feb;65(2):313-9.

HABAs Can Be Significant Source of POPs



Duty SM, et al. Personal care product use predicts urinary concentrations of some phthalate monoesters. Environ Health Perspect. 2005 Nov;113(11):1530-5

Breast Feeding Decreases POPs



Bjermo H, et al. Fish intake and breastfeeding time are associated with serum concentrations of organochlorines in a Swedish population. Environ Int. 2013 Jan;51:88-96

FACILITATE DETOXIFICATION AND EXCRETION

Mediterranean Diet Slows Aging and Prevents Neurological disease

- Those following most closely this dietary pattern have a longer lifespan and a **reduced risk of neurodegenerative disease, including Alzheimer's**
- Review of all prospective cohort studies (nearly 600,000 subjects)
- Greater adherence to a Mediterranean diet is associated with a significant reduction in:
  - Overall mortality (-8%),
  - Mortality/incidence of cardiovascular diseases (-10%),
  - Incidence of or mortality from cancer (-6%),
  - **Incidence of Parkinson's disease and Alzheimer's disease (-13%)**

Pérez-López FR, Chedraui P, Haya J, Cuadros JL. Effects of the Mediterranean diet on longevity and age-related morbid conditions. Maturitas. 2009 Oct 20;64(2):67-79. Epub 2009 Aug 31.
Sofi F, et al. Adherence to Mediterranean diet and health status: meta-analysis. Am J Clin Nutr. 2010 Nov;92(5):1189-96.

Fiber Decreases POPs

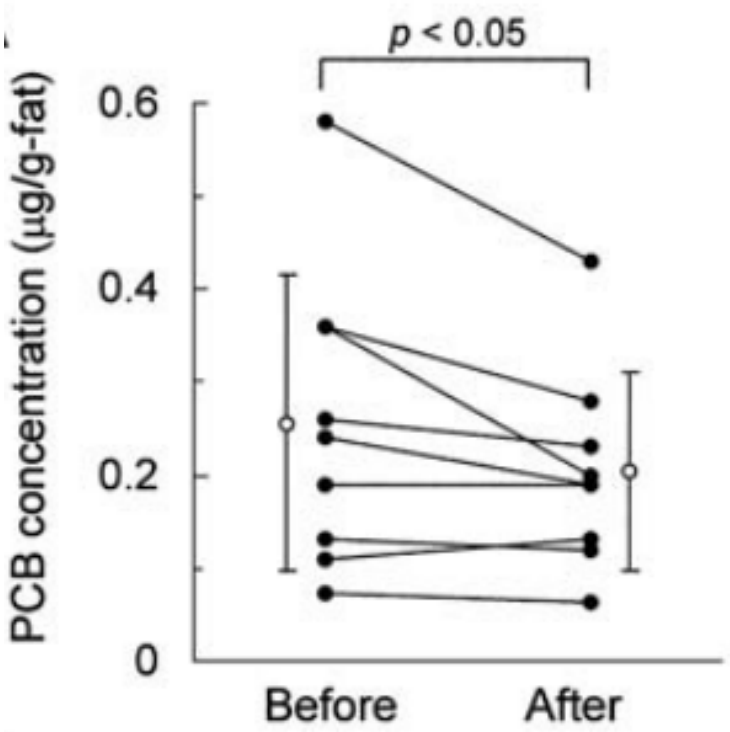
- Fiber
  - Rice bran (PCBs, PCDFs, dioxins)
  - Wheat bran (PCBs)
  - 5g/day
  - Slow!!
- Bile sequestrants
  - Cholestamide, Cholestyramine, Olestra

Sera N, et al. Binding effect of polychlorinated compounds and environmental carcinogens on rice bran fiber. J Nutr Biochem. 2005 Jan;16(1):50-8

Genuis SJ, Birkholz D, Ralitsch M, Thibault N. Human detoxification of perfluorinated compounds. Public Health, 2010; 124:367–75

Colestimide Reduces PCBs

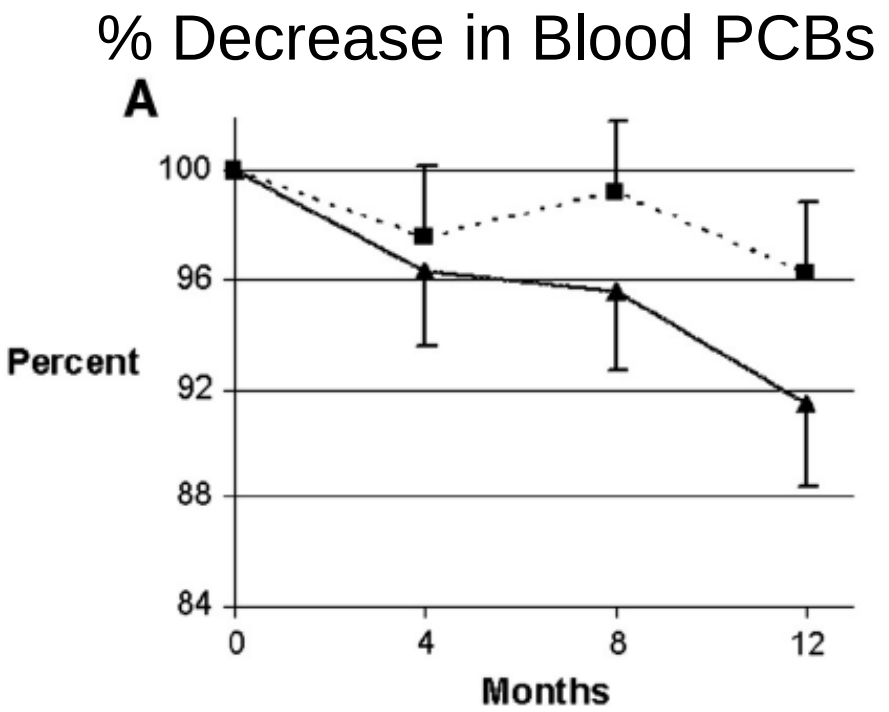
- 5 g/d (?)
- 6 months
- Average reduction 23%
- Those who did not take increased 24%



Sakurai K, Fukata H, Todaka E, et al. Colestimide reduces blood polychlorinated biphenyl (PCB) levels. Intern Med. 2006;45(5):327-8

Olestra Decreases PCBs and DDE

- Potato chips made with olestra or vegetable oil
- 12 months
- 15 g of olestra per day
  - 22 Pringles Light crisps
- No change in diet
- Higher body fat = lower % decrease
- 25% loose stools

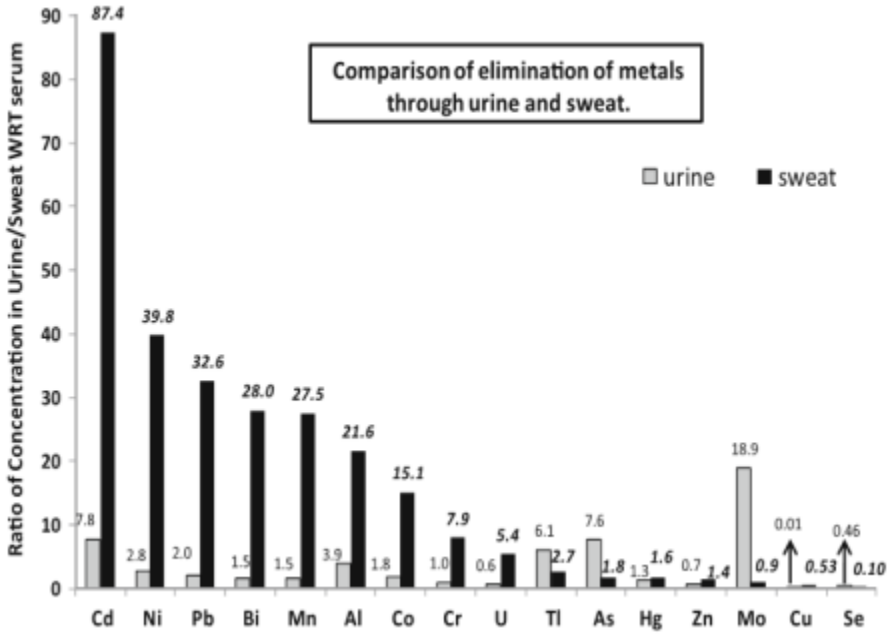


½ life decreased from 20+ years to 8.5 years

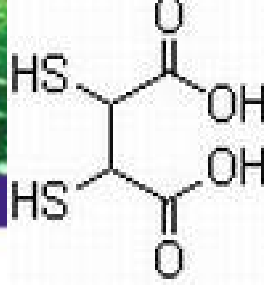
Jandacek RJ, Heubi JE, Buckley DB, et al. Reduction of the body burden of PCBs and DDE by dietary intervention in a randomized trial. J Nutr Biochem, 2014;25 483–488

Cadmium – Sweat it Out!

- **Cadmium eliminated efficiently through sweat**
- 20 individuals sweat via exercise, steam or infrared sauna
- Cadmium found in sweat in those with undetectable serum levels, suggesting it could be used for assessment of burden
- Elimination of other minerals (Cu, Mn) suggests need replenishment during induced sweat



Genuis SJ, et al. Blood, Urine, and Sweat (BUS) Study: Monitoring and Elimination of Bioaccumulated Toxic Elements. Arch Environ Contam Toxicol. 2011 Aug;61(2):344-57



DMSA to Excrete Lead and Mercury

- 2,3-Dimercaptosuccinic acid
- SH-containing, water-soluble, low-toxicity, oral (IV toxic)
- Developed in 1950s as alternative to more toxic chelating agents
- 10-20% of oral dose absorbed
- Chelates all forms of mercury (more effective for Pb)
- ½ through urine, ½ through bile
- Amount of Hg bound: ~7.5 ug/g of oral DMSA
- Increases glutathione production
- ½ life in blood 2-3 hours

Ruha AM, Curry SC, Gerkin RD, et al. Urine mercury excretion following meso-dimercaptosuccinic acid challenge in fish eaters. Arch Pathol Lab Med. 2009 Jan;133(1):87-92

Roels HA, Boeckx M, Ceulemans E, Lauwerys RR. Urinary excretion of mercury after occupational exposure to mercury vapour and influence of the chelating agent meso-2,3-dimercaptosuccinic acid (DMSA). Br J Ind Med. 1991 Apr;48(4):247-53

DMSA

- Nutrients to improve efficacy
  - Alpha lipoic acid
  - NAC
  - Probiotics
  - Fiber
- Research studies use 30 mg/kg/day
  - 7 days on, 7 off
  - Not recommended
- Protocol we used:
  - 50 mg trial dose; if no reaction within 2 hours:
    - 250 mg qd for 3 days then off for 11 days, or
    - 250 mg every 3rd day before bed

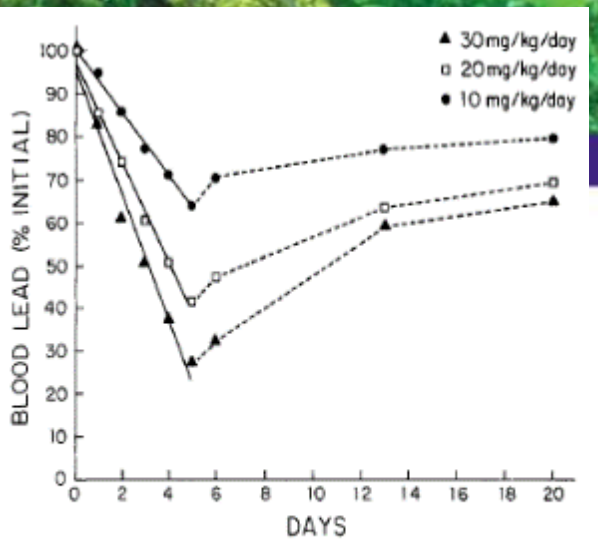
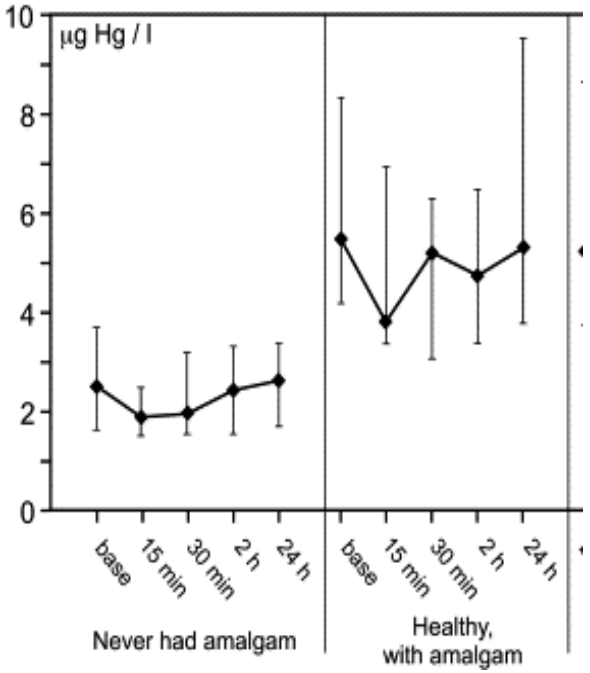


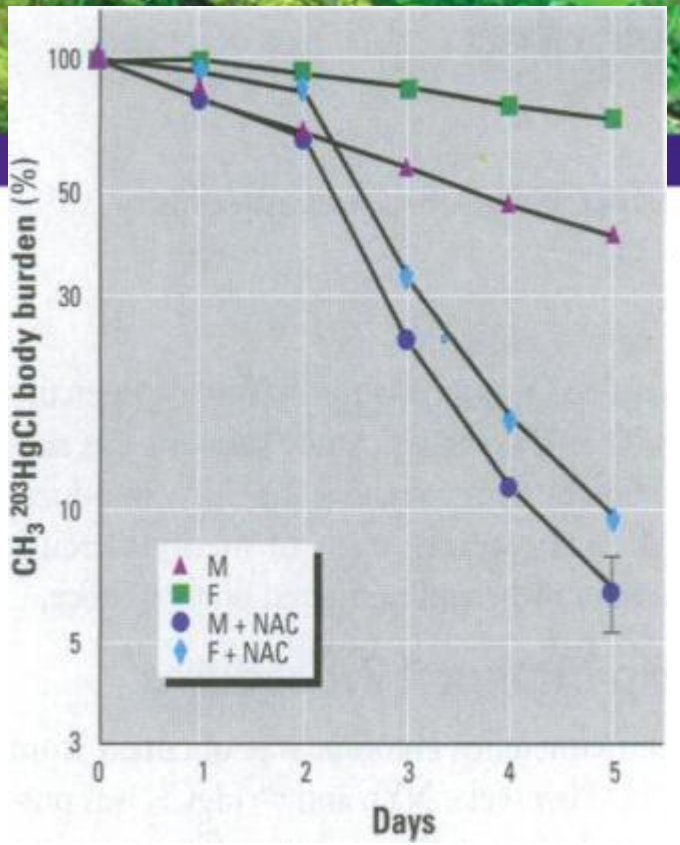
Fig. 1. Mean BPb concentration (expressed as percentage of pretreatment value) after 5 days of DMSA therapy.

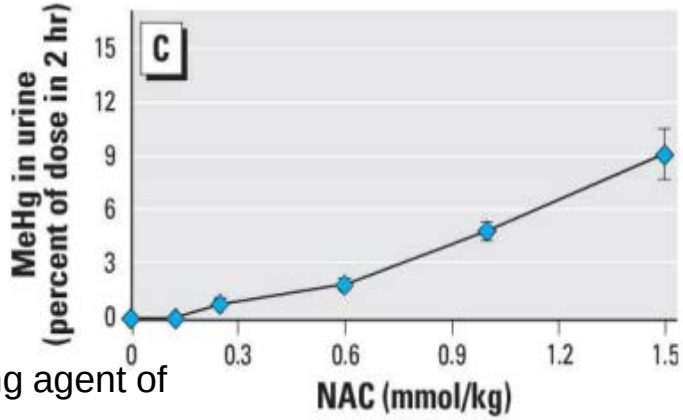


Graziano JH, et al. 2,3-Dimercaptosuccinic acid as an antidote for lead intoxication. Clin Pharmacol Ther. 1985;37(4):431-8

NAC

- Most research animal and human cell lines
- Multiple benefits:
  - Increases production of glutathione
  - Protects human neurological cells from Hg toxicity
  - Reverses damage to human pancreatic cells from Hg
  - Directly binds to Hg, esp. MeHg, and excrete through kidneys





Aremu DA, et al. N-acetylcysteine as a potential antidote and biomonitoring agent of methylmercury exposure. Environ Health Perspect. 2008 Jan;116:26-31

Ballatori N, et al. N-acetylcysteine as an antidote in methylmercury poisoning. Environ Health Perspect. 1998 May;106:267-71

Watch for Sulfur Sensitive Patients

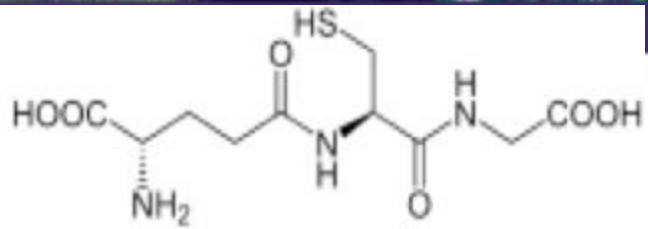
- Clinical indications:
  - Allergies — Onion and/or garlic intolerance
  - GURD — Sulfite sensitivity
  - IBS
- Laboratory:
  - Increased sulfite/sulfate ratio in urine
  - Decreased Phase II sulfation
- Intervention:
  - Molybdenum 300 ug/d
  - Manganese 20 mg/d
- DMSA and possibly NAC contraindicated until S metabolism improved

Lead Detoxification

- Chelators: DMPS, DMSA, EDTA, d-penicillamine (DPA)
  - Long history of EDTA use, most often used IV
  - EDTA also depletes Zn, Cu, Fe, Co, and Mn
  - **Oral DMSA as effective as IV EDTA**
    - Pt example decreased from 3.7 to 2.4
  - Not clear if DMSA removes lead from bone, but does reduce hippocampal lead
  - Combination of EDTA and DMSA increase excretion

Bradberry, S et al. A comparison of sodium calcium edetate (edetate calcium disodium) and succimer (DMSA) in the treatment of inorganic lead poisoning. Clinical Toxicology 2009
Bradberry Use of oral DMSA in adult patients with inorganic lead poisoning. QJM. 2009
Lee BK, Provocative chelation with DMSA and EDTA: evidence for differential access to lead storage sites. Occup Environ Med. 1995

Glutathione: Critical



- **Difficult to overstate its importance in brain health**
- Most important intracellular and intra-mitochondrial antioxidant
- Binds and transports mercury out of cells and brain
- Irreversibly(?) binds to mercury in the brain
- Neutralizes oxidative damage from mercury and POPs
- Facilitates detoxification of POPs
- Depleted by oxidative stress, metals, alcohol
- Even predictor of healthy aging!

Baker, SM. The Metaphor of Oceanic Disease. IMCJ February, 2008;7:1.
Mosharov, E., Cranford, M.R., Baneriee, R. The Quantitatively Important Relationship between Homocysteine Metabolism and Glutathione Synthesis by the Transsulfuration Pathway and Its Regulation by Redox Changes. Biochemistry. 2000 Sept;39:13005-13011.

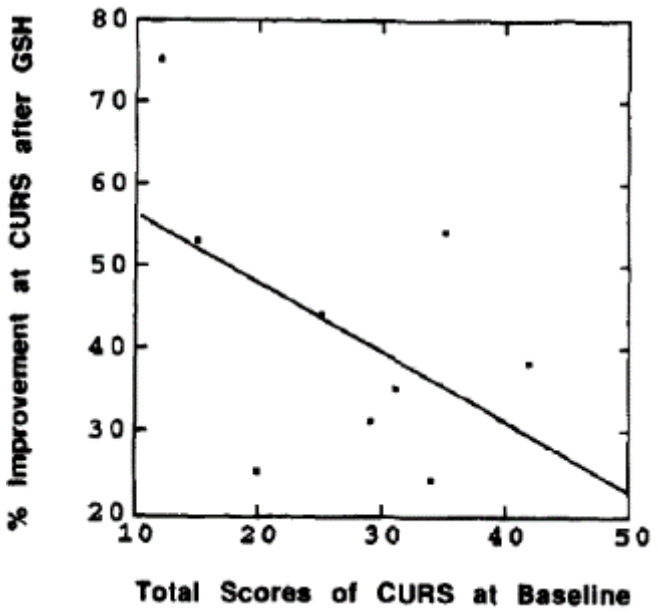
Depleted GSH Has Been Implicated In:

- Neurodegenerative disorders (Alzheimer's, Parkinson's and Huntington's diseases, amyotrophic lateral sclerosis, Friedreich's ataxia)
- Pulmonary disease (COPD, asthma, and acute respiratory distress syndrome)
- Immune diseases (HIV, autoimmune disease)
- Cardiovascular diseases (hypertension, myocardial infarction, cholesterol oxidation)
- Liver disease
- Cystic fibrosis
- Chronic age-related diseases (cataracts, macular degeneration, hearing impairment, and glaucoma)
- Aging process itself

Ballatori N, Krance SM, Notenboom S, Shi S, Tieu K, Hammond CL. Glutathione dysregulation and the etiology and progression of human diseases. Biol Chem. 2009 Mar;390(3):191-214

Glutathione Protects Neurons

- 50% less glutathione (GSH) in the substantia nigra of Parkinson's patients
- But not in other parts of brain => used up in neutralization of local toxins
- GSH 600 mg IV bid x 30 days
  - 42 % decline in disability
  - Lasted 2-4 months after stopped
- **Protects both telomeres and mtDNA**

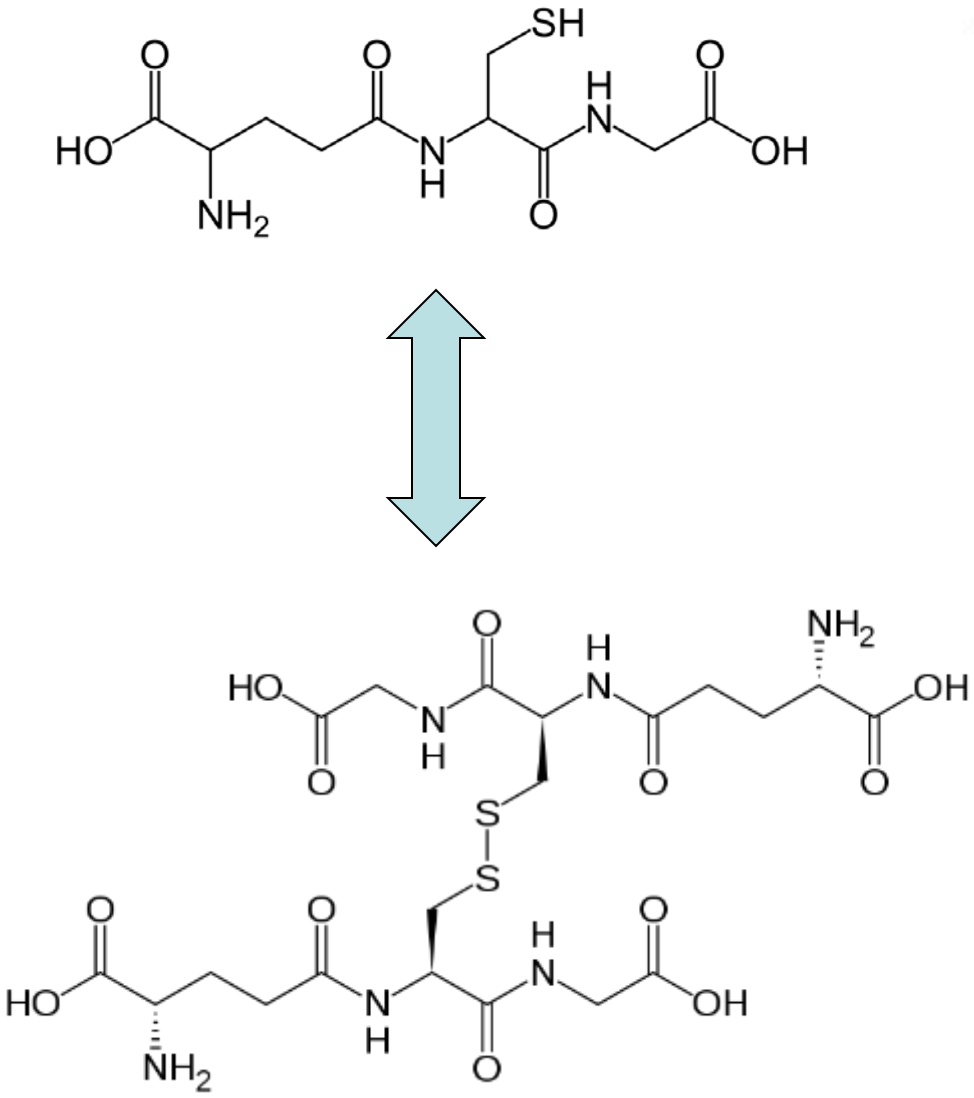


Perry TL, et al. Idiopathic Parkinson's disease: A disorder due to nigral glutathione deficiency. Neuroscience Letter 1986;67:269-74

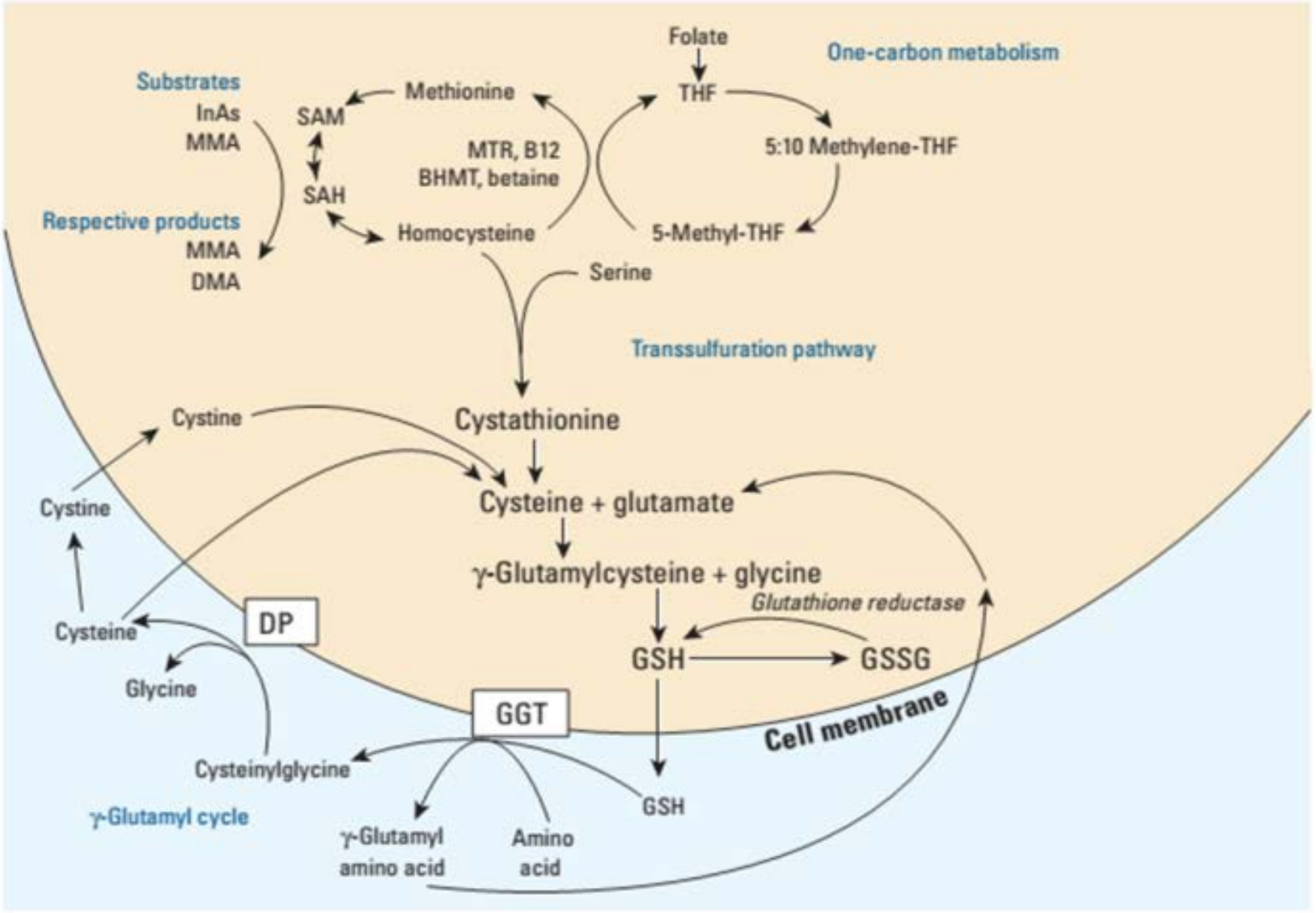
Sechi G, et al. Reduced intravenous glutathione in the treatment of early Parkinson's disease. Prog Neuropsychopharmacol Biol Psychiatry 1996;20:1159-70

Glutathione

- Tripeptide (cysteine, glycine and glutamic acid)
- Relatively high (**5 millimolar**) concentrations in most cells
- Exists in reduced state (GSH) and oxidized state (GSSG)
- Ratio determines cell redox status
  - **Healthy cells at rest have a GSH/GSSG ratio >100**
  - Ratio drops to 1-10 in cells exposed to oxidant stress
- **Produced exclusively in the cytosol and actively pumped into mitochondria**



Synthesis, Regeneration and Recycling

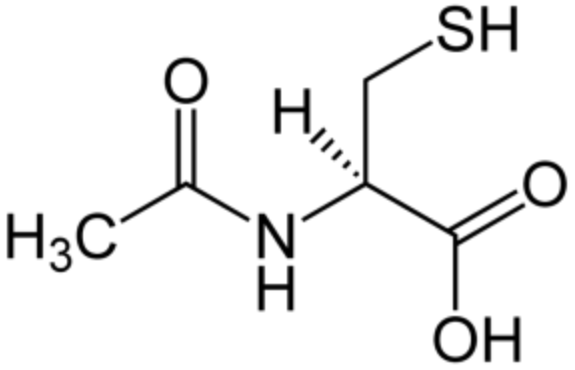


Hall MN, Niedzwiecki M, Liu X, et al. Chronic arsenic exposure and blood glutathione and glutathione disulfide concentrations in bangladeshi adults. Environ Health Perspect. 2013 Sep;121(9):1068-74

Glutathione: Direct Administration

- IV glutathione
- Nebulized glutathione
- Oral glutathione (basically, expensive cysteine)
- Oral liposomal glutathione
- Topical glutathione
- Intranasal glutathione

Allen J, Bradley RD. Effects of oral glutathione supplementation on systemic oxidative stress biomarkers in human volunteers. J Altern Complement Med. 2011 Sep;17(9):827-33.
Cooke RW, Drury JA. Reduction of oxidative stress marker in lung fluid of preterm infants after administration of intra-tracheal liposomal glutathione. Biol Neonate. 2005;87(3):178-80
Buhl R, et al. Augmentation of glutathione in the fluid lining the epithelium of the lower respiratory tract by directly administering glutathione aerosol. Proc Natl Acad Sci USA 1990;87:4063–7
Kern JK, et al. A clinical trial of glutathione supplementation in autism spectrum disorders. Med Sci Monit. 2011 Dec;17(12):CR677-82.



NAC Elevates Glutathione

- N-acetylcysteine
- Amino acid cysteine is a rate-limiting factor for GSH synthesis
- Variety of both clinical trials and in-vitro/in-vivo data suggest that supplying cysteine as NAC is an effective strategy for enhancing GSH production and intracellular cysteine.
- Increases intracellular glutathione
- **Dosage dependent increase in glutathione**

Dodd S, Dean O, Copolov DL, Malhi GS, Berk M. N-acetylcysteine for antioxidant therapy: pharmacology and clinical utility. Expert Opin Biol Ther. 2008 Dec;8(12):1955-62

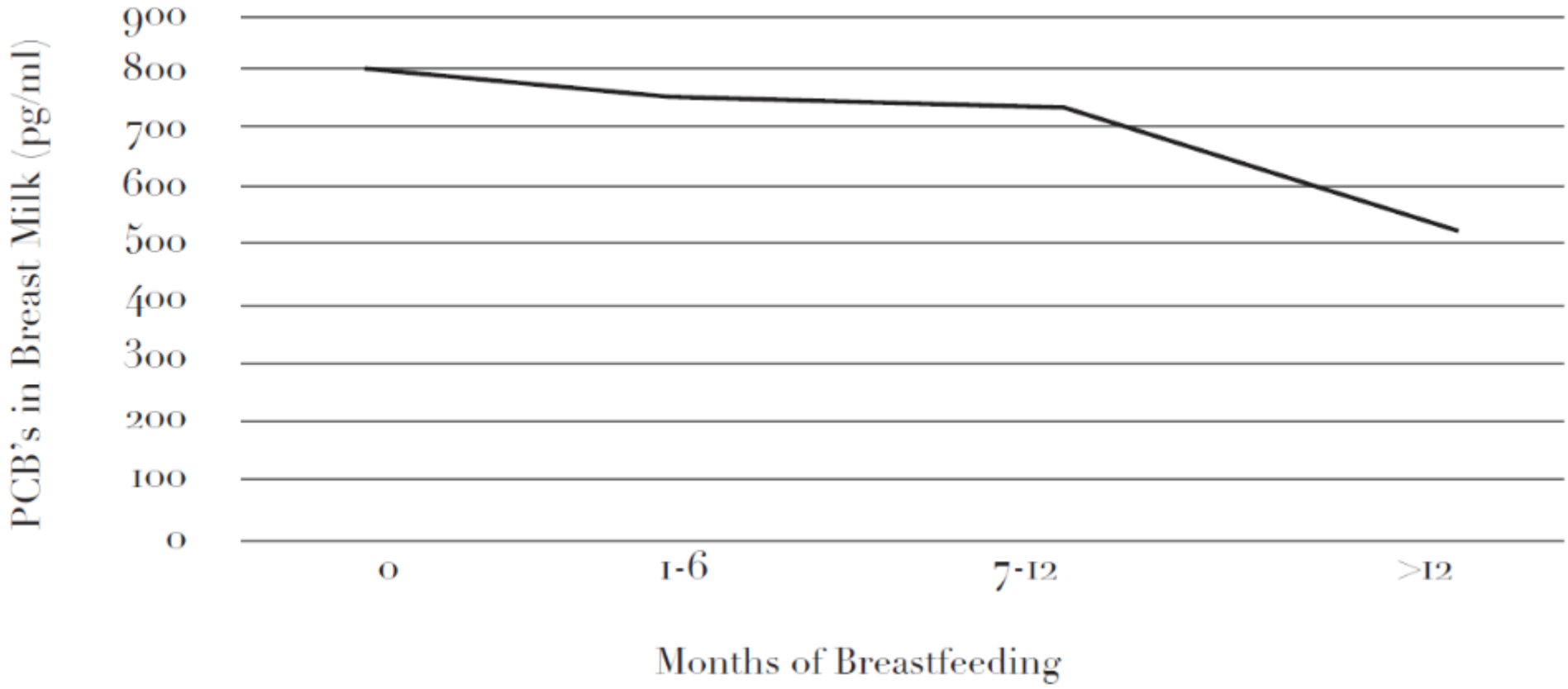
Soltan-Sharifi MS, et al. Improvement by N-acetylcysteine of acute respiratory distress syndrome through increasing intracellular glutathione, and extracellular thiol molecules and anti-oxidant power: evidence for underlying toxicological mechanisms. *Hum Exp Toxicol. 2007 Sep;26(9):697-703.*

NAC Decreases GGT

- 600mg/day for 4 weeks reduced GGT from 62.7 to 46.3 U/L.
- Expected result as decreases need for recycling glutathione

Pamuk GE, Sonsuz A. N-acetylcysteine in the treatment of non-alcoholic steatohepatitis. J Gastroenterol Hepatol. 2003;18(10):1220-1

Breast Feeding Decreases PCBs



Case Histories

Patience!

Don’t expect the speed of results seen with drug or even nutrition therapy

1. First must greatly decrease body load
   - Decrease exposure as much as possible
   - Some toxins become apparent only after others removed
2. For damaged enzymes to work:
   - Must displace enzyme poison with nutrient cofactor, or
   - Degrade and replace enzyme
     - **½ life MAO-B in baboon brain = 30 days**
3. Then the tissue damage has to be repaired

Arnett CD, Fowler JS, MacGregor RR, et al. Turnover of brain monoamine oxidase measured in vivo by positron emission tomography using L-[11C]deprenyl. J Neurochem. 1987;49:522-7

It All Started After Amalgams (MB)

48 yo male, employee, Calgary

Relevant medical history

- Symptoms began 2 mo after amalgams and gold crowns
- Chest pain followed by weakness, dizziness and shortness of breath.
- Multiple trips to emergency room with no answers.
- Neck pain, gastrointestinal problems and insomnia. Extreme fatigue, chronic sinusitis.
- 8 amalgams, 2 gold crowns
- Challenge Hg: 5.8 ug/g creat

Intervention

- All amalgams removed
- B-complex
- Vitamin C
- Infrared saunas
- IV DMPS

Results

- “Feel better now both physically and mentally than I have in 15 years.”
- Virtually all symptoms eventually alleviated
- All prescription drugs discontinued
- Improvement within 2 weeks of removal of amalgams

Bertsch M. A patient’s report of mercury poisoning. IMCJ 2010;9:14-15

MB Symptoms That Went Away

- Chest pains
- Completely exhausted all the time
- Amalgam tattooing on the gums
- **Muscle twitching and muscle tremors**
- Burning in the mouth and tongue
- **Numbness in the feet and hands- feeling of something crawling under the skin**
- **Insomnia**
- Night Sweats
- **Tingling on the face**
- **Tingling and prickly feeling on the scalp and legs**
- Severe lower back pain
- Sore muscles and joint pain
- **Double vision**
- **Blurred vision**
- Jabbing pain in the eyes
- **Dizziness**
- **Depression**
- **Anxiety – panic attacks**
- **Memory loss**
- **Brain fog – impaired cognitive thinking**
- Sour and metallic taste
- Increased saliva production
- Elevated liver enzymes
- Itchy hands
- High pitch whining in the ears
- Persistent cough and sore throat
- Cold hands and feet
- No appetite to eat

Full relief took ~ 2 years

Am I Losing my Mind? April 2012

- 67 yo white woman
- *I had the odd feeling that I was living in a fog, that things were very fuzzy and that my memory was very sporadic. I was having trouble sleeping and had a lot of muscle aches during the night. I always had a metal taste in my mouth and felt that my breath lacked freshness other than the first few minutes after brushing my teeth. My skin and scalp were always sore and especially dry.*

2 years IV chelation discontinued due to side effects & no benefit

Toxic Metals; Urine APR 2 0 2012

TOXIC METALS

		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	3.4	< 35	
Antimony	(Sb)	< dl	< 0.4	
Arsenic	(As)	27	< 117	
Barium	(Ba)	6.9	< 7	
Beryllium	(Be)	< dl	< 1	
Bismuth	(Bi)	< dl	< 15	
Cadmium	(Cd)	0.4	< 1	
Cesium	(Cs)	7.7	< 10	
Gadolinium	(Gd)	0.3	< 0.4	
Lead	(Pb)	3.7	< 2	
Mercury	(Hg)	50	< 4	
Nickel	(Ni)	4.4	< 12	
Palladium	(Pd)	< dl	< 0.3	
Platinum	(Pt)	< dl	< 1	
Tellurium	(Te)			
Thallium	(Tl)			
Thorium	(Th)			
Tin	(Sn)			
Tungsten	(W)	< dl	< 0.4	
Uranium	(U)	< dl	< 0.04	

Hg = 50!

URINE CREATININE

	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	33.1	35- 225	

SPECIMEN DATA

Comments:

Date Collected: 3/22/2012
Date Received: 3/29/2012
Date Completed: 4/3/2012
Method: ICP-MS

pH upon receipt: Acceptable
<dl: less than detection limit
Provoking Agent: DMPS
Creatinine by Jaffe Method

Collection Period: timed: 6 hours
Volume: 1500 ml
Provocation: POST PROVOCATIVE

Results are creatinine corrected to account for urine dilution variations. **Reference intervals and corresponding graphs are representative of a healthy population under non-provoked conditions.** Chelation (provocation) agents can increase urinary excretion of metals/elements. V13

November 2012

- *I do know that things really improved once I started your protocol and I was happy to see the light at the end of the Mercury tunnel.*

Toxic Metals; Urine

TOXIC METALS		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	19	< 35	
Antimony	(Sb)	0.3	< 0.4	
Arsenic	(As)	27	< 117	
Barium	(Ba)	10	< 7	
Beryllium	(Be)	< dl	< 1	
Bismuth	(Bi)	< dl	< 15	
Cadmium	(Cd)	0.6	< 1	
Cesium	(Cs)	8.9	< 10	
Gadolinium	(Gd)	< dl	< 0.4	
Lead	(Pb)	4.3	< 2	
Mercury	(Hg)	12	< 4	
Nickel	(Ni)	7.2	< 12	
Palladium	(Pd)	< dl	< 0.3	
Platinum	(Pt)	< dl	< 1	
Tellurium	(Te)			
Thallium	(Tl)			
Thorium	(Th)			
Tin	(Sn)			
Tungsten	(W)	< dl	< 0.4	
Uranium	(U)	< dl	< 0.04	

Hg = 12

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	23.6	35 - 225	

SPECIMEN DATA

Comments:

Date Collected: 10/23/2012
Date Received: 10/30/2012
Date Completed: 10/31/2012
Method: ICP-MS

pH upon receipt: Acceptable
<dl: less than detection limit
Provoking Agent: DMPS
Creatinine by Jaffe Method

Collection Period: timed: 6 hours
Volume: 2100 ml
Provocation: POST PROVOCATIVE

Results are creatinine corrected to account for urine dilution variations. **Reference intervals and corresponding graphs are representative of a healthy population under non-provoked conditions.** Chelation (provocation) agents can increase urinary excretion of metals/elements.

V13

June 2013

- *With each successive test the symptoms were lessening and I was feeling more normal.*

Toxic Metals; Urine

TOXIC METALS

		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	13	< 35	
Antimony	(Sb)	0.3	< 0.2	
Arsenic	(As)	13	< 80	
Barium	(Ba)	11	< 7	
Beryllium	(Be)	< dl	< 1	
Bismuth	(Bi)	< dl	< 4	
Cadmium	(Cd)	0.5	< 1	
Cesium	(Cs)	11	< 10	
Gadolinium	(Gd)	< dl	< 0.8	
Lead	(Pb)	2.8	< 2	
Mercury	(Hg)	7.3	< 4	
Nickel	(Ni)	4.6	< 10	
Palladium	(Pd)	< dl	< 0.15	
Platinum	(Pt)	< dl	< 0.1	
Tellurium	(Te)			
Thallium	(Tl)			
Thorium	(Th)			
Tin	(Sn)			
Tungsten	(W)	< dl	< 0.4	
Uranium	(U)	< dl	< 0.04	

Hg = 7.3

URINE CREATININE

	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	26.6	35- 225	

SPECIMEN DATA

Comments:

Date Collected: 05/21/2013
Date Received: 05/23/2013
Date Completed: 05/28/2013
Method: ICP-MS

pH upon receipt: Acceptable
<dl: less than detection limit
Provoking Agent: DMPS
Creatinine by Jaffe Method

Collection Period: timed: 6 hours
Volume: 2000 ml
Provocation: POST PROVOCATIVE

Results are creatinine corrected to account for urine dilution variations. **Reference intervals and corresponding graphs are representative of a healthy population under non-provoked conditions.** Chelation (provocation) agents can increase urinary excretion of metals/elements.

V13

December 2013

- *It was a day of celebration when I received the last test results.*
- *I would **caution people to remember that clearing mercury out of one's system is a long process** but it is worth the effort even if it takes many years. Being healthy is a good reward for all the patience required to do the heavy mercury lifting.*
- *Good luck with your seminars. I will always be in your debt for your help.*

Toxic Metals; Urine

TOXIC METALS

		RESULT µg/g creat	REFERENCE INTERVAL	WITHIN REFERENCE / OUTSIDE REFERENCE
Aluminum	(Al)	2.6	< 35	
Antimony	(Sb)	< dl	< 0.2	
Arsenic	(As)	12	< 80	
Barium	(Ba)	27	< 7	
Beryllium	(Be)	< dl	< 1	
Bismuth	(Bi)	< dl	< 4	
Cadmium	(Cd)	0.4	< 1	
Cesium	(Cs)	7.9	< 10	
Gadolinium	(Gd)	< dl	< 0.8	
Lead	(Pb)	2.4	< 2	
Mercury	(Hg)	3.5	< 4	
Nickel	(Ni)	4.2	< 10	
Palladium	(Pd)	< dl	< 0.15	
Platinum	(Pt)	< dl	< 0.1	
Tellurium	(Te)			
Thallium	(Tl)			
Thorium	(Th)			
Tin	(Sn)			
Tungsten	(W)	< dl	< 0.4	
Uranium	(U)	< dl	< 0.04	

Hg = 3.5!

URINE CREATININE

	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	29.1	40- 225	

SPECIMEN DATA

Comments:

Date Collected: 12/17/2013
Date Received: 12/19/2013
Date Completed: 12/20/2013
Method: ICP-MS

pH upon receipt: Acceptable
<dl: less than detection limit
Provoking Agent: DMPS
Creatinine by Jaffe Method

Collection Period: timed: 6 hours
Volume:
Provocation: POST PROVOCATIVE

Results are creatinine corrected to account for urine dilution variations. **Reference intervals and corresponding graphs are representative of a healthy population under non-provoked conditions.** Chelation (provocation) agents can increase urinary excretion of metals/elements.

V13

Summary: Assessment

Metals

- First morning urine (current exposure)
- Challenge with, oral:
  - DMSA 500mg
  - DMPs 300 mg
  - Collect urine 6 hours

(body load)

Chemicals and POPs

- Urine or blood

Total Toxic Load

- GGT: > 25 (20?)
- 8-OHdG: >4 ng/mg creat

Summary: Intervention

1. Keep the toxins out!
   - Organically grown foods
   - Prepare own food
   - Food stored in glass, not plastic or cans
   - Clean water
   - Safe health and beauty aids
2. Facilitate detoxification and excretion
   - High fiber diet and supplements
   - Good quality multivitamin and mineral
   - DMSA if lead or mercury
3. Protects against damage
   - NAC to increase glutathione to protect against oxidative and damage and for binding POPs

4 Generations

Diet	Mediterranean	Med/Amer	American	Mediterranean
Toxins	Low	Moderate	High	Moderate
Supplements	None	None	None	Sophisticated
Age	95	95	88	??
Vitality	High	Moderate	Debilitated	BB 3x/wk
Chr Disease	None	Some	Dementia Heart Dz Osteoarthritis Osteoporosis	None

Motorcycling Australia on the "Wrong Side of the Road"

Summary

1. Toxins are now ubiquitous in the industrialized world
2. Toxins are now the primary drivers of chronic disease
3. Standard laboratory tests now include in “normal” range the body’s adaptations to, and damage from, toxins

Thank you

Chrissie Cirovic, ND & Geoff Bender, ND

For Your Excellent Research Work