Fullscript

Environmental medicine

Practical guidance for leveraging environmental medicine in your practice.

Fullscript

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Co-Author, Clinical Environmental Medicine
Fullscript Medical Advisory Board

Learning Objectives

After participating in this presentation, learners will be better able to:

- Understand the 5 toxins that contribute the most to common chronic diseases according to current research.
- Recognize the clinical manifestation of these toxins in patients.
- Identify laboratory tests for assessment of body load of persistent and non-persistent toxins.
- Help patients decrease exposure to these toxins.
- Effectively increase elimination of these toxins.

Overview

- Worldwide epidemic of chronic disease
- Causes and risk factors: type 2 diabetes
- Bioaccumulation of top 5 environmental toxins
  - Diseases caused
  - Common sources
  - Assessment
  - Intervention: avoidance and elimination strategies
- Summary

Presentation data

- All human data
- Primarily U.S. data, as a lot more research is available
- Spot checking toxins in other countries shows the same toxin overload, but variations in which are most prevalent:
  - Australia (higher PBDEs)
  - Canada (higher lead)
  - New Zealand (higher cadmium)
  - Sweden (higher most toxic metals)
  - UK (highest PDBEs in world, 3x OCP of US)

Converting disease risk to % of disease due to toxins

Attributable fraction (AF) calculation

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

p = underlying prevalence of risk factor in the population.

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

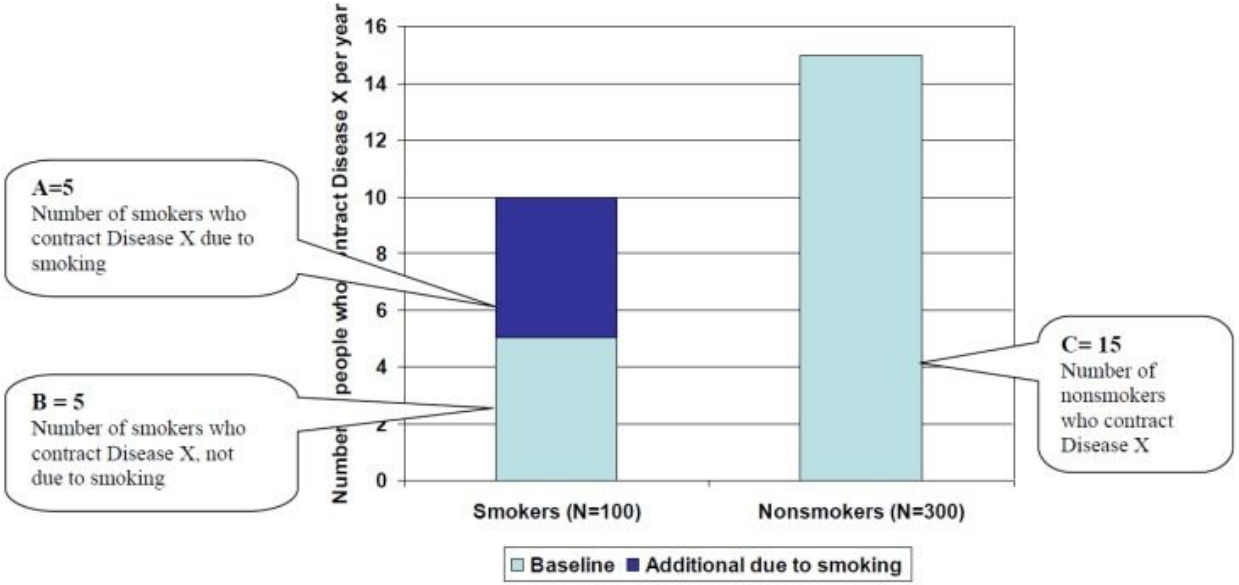
AF = % of disease due to the toxin.

Levin, M. L., (1953). The occurrence of lung cancer in man.

AF calculation: disease risk due to smoking

Number of smokers and nonsmokers who contract disease.

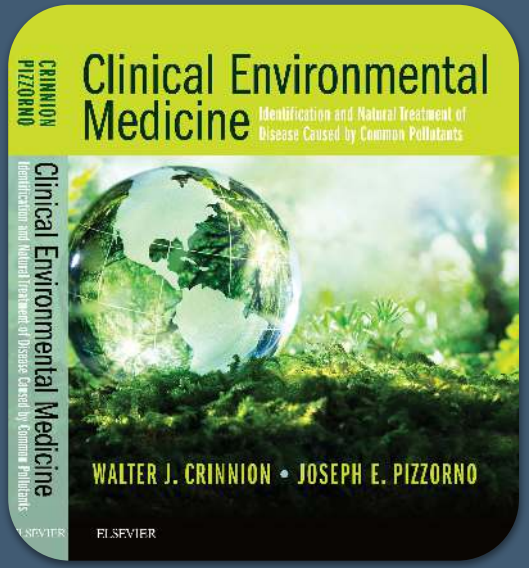
$$AF = \frac{A}{A + B + C}$$



[Rosen, L. (2013). An intuitive approach to understanding the attributable fraction of disease due to a risk factor: the case of smoking.]

The branch of medicine that deals with diagnosing and caring for people exposed to chemical and physical hazards … through such media as contaminated soil, water, and air.

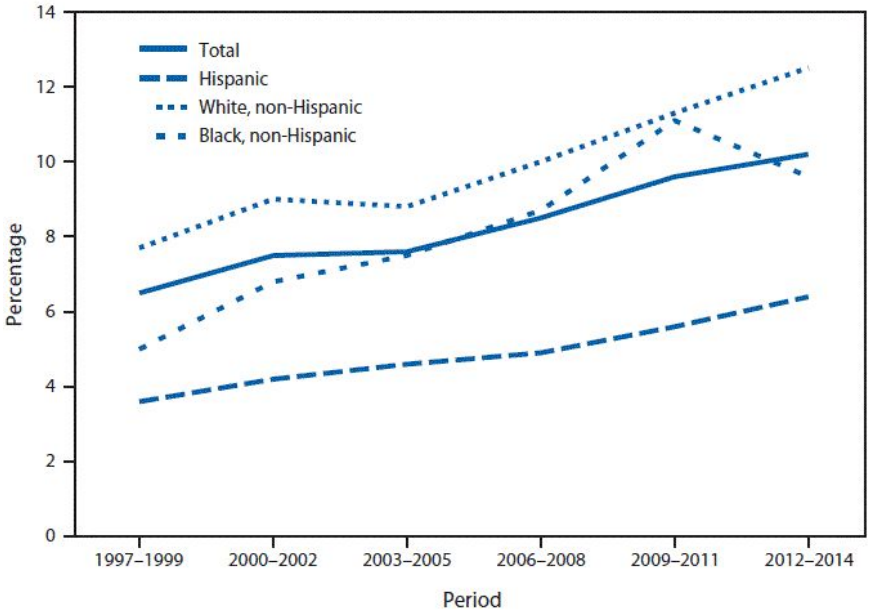
- Clinical Environmental Medicine



Worldwide epidemic of chronic disease

ADHD

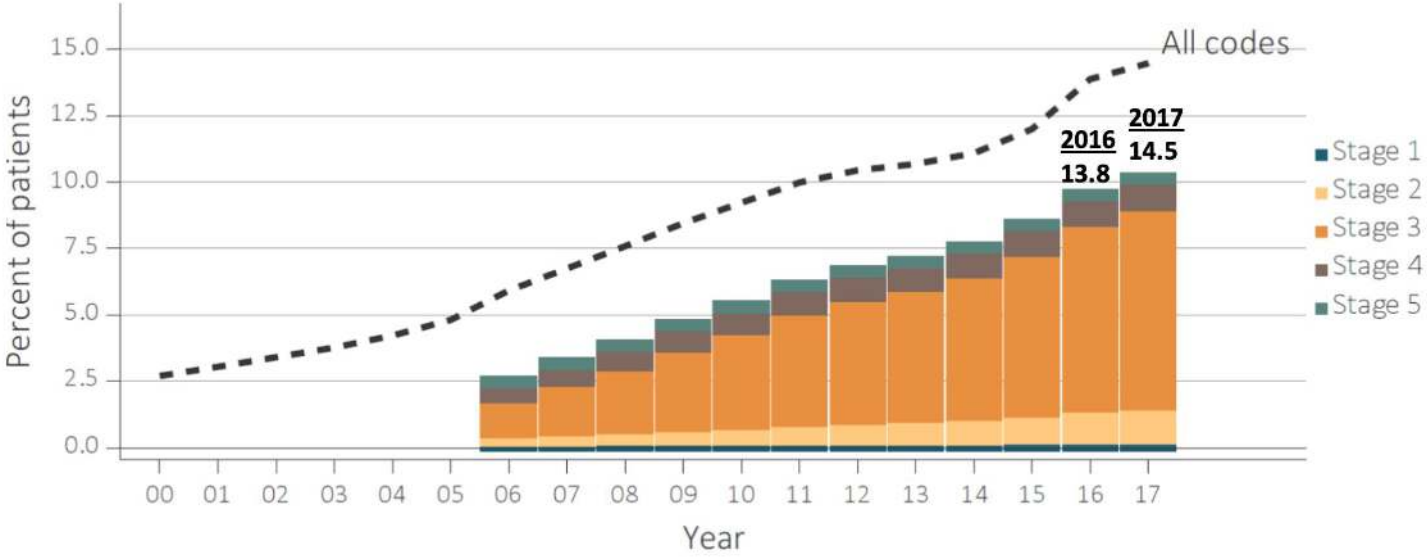
Percentage of children and adolescents aged 5–17 years with diagnosed Attention-Deficit/ Hyperactivity Disorder (ADHD), United States, 1997–2014.



Centers for Disease Control and Prevention. (2015). QuickStats.

Kidney disease

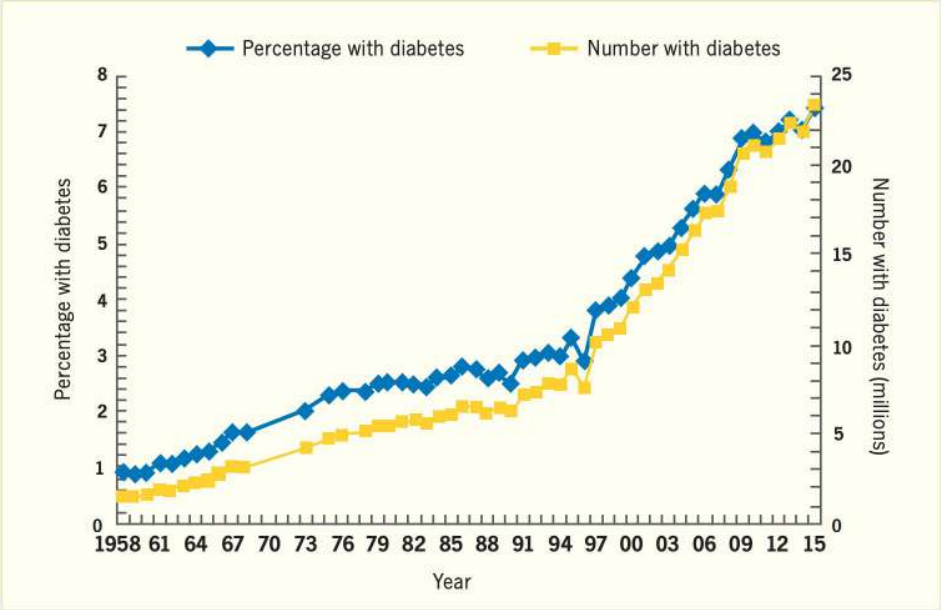
Trends in prevalence of recognized chronic kidney disease (CKD), overall and by CKD stage, among Medicare patients (aged 65+ years), 2000-2017.



United States Renal Data System. (2019). US Renal Data System 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States.

Diabetes

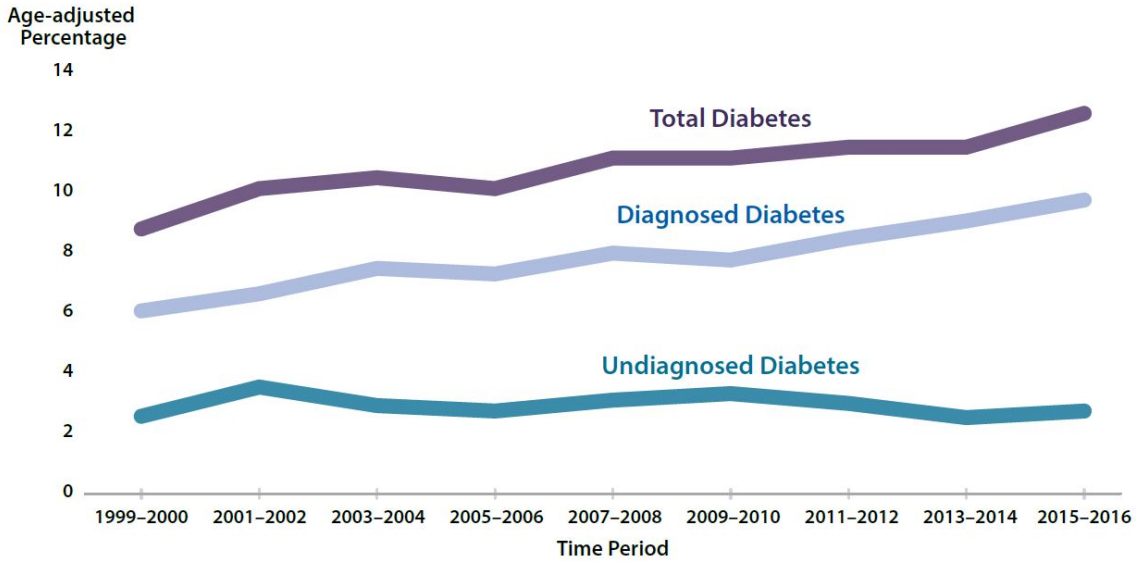
Number and percentage of the U.S. population with diagnosed diabetes, 1958–2015.



[National Institute of Diabetes and Digestive and Kidney Diseases. (2018). Diabetes in America, 3rd Edition.]

Diabetes

Trends in age-adjusted prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 1999–2016.

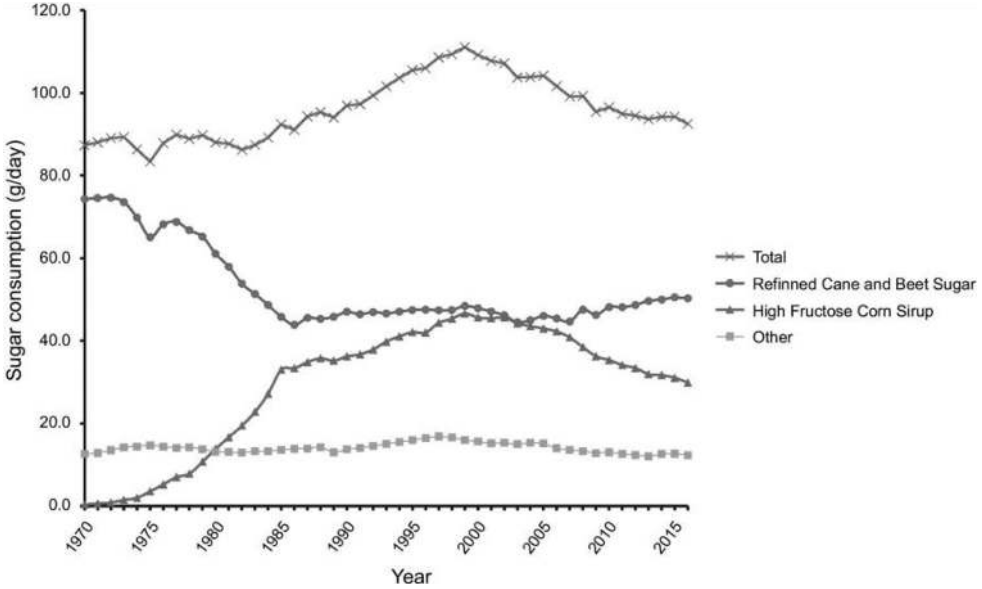


Centers for Disease Control and Prevention. (2020). Prevalence of both diagnosed and undiagnosed diabetes.

Causes and risk factors: type 2 diabetes

Sugar?

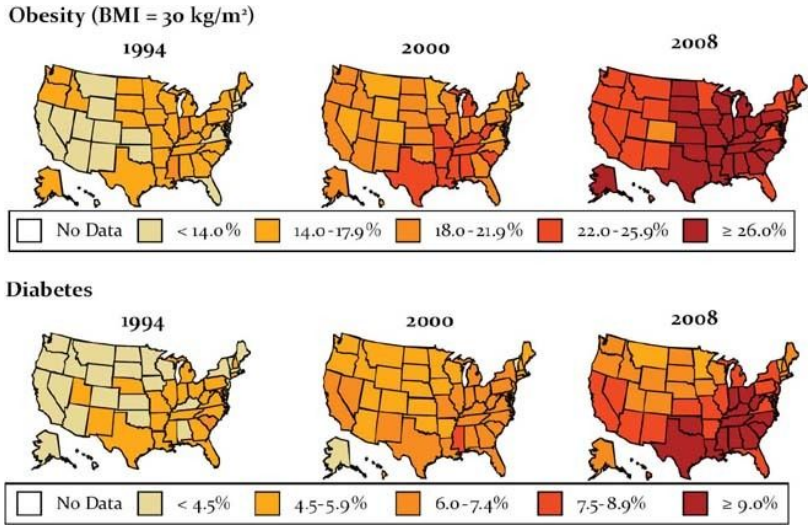
Per capita sugar consumption for total, refined cane and beet sugar, high fructose corn syrup, and other sugars (molasses, honey, etc.) in grams per day from 1970 to 2016.



[Faruque, S., et al. (2019). The dose makes the poison: Sugar and obesity in the United States – a review.]

Obesity?

Age-adjusted percentage of U.S. adults who were obese or who had a diagnosis of diabetes mellitus.



However...

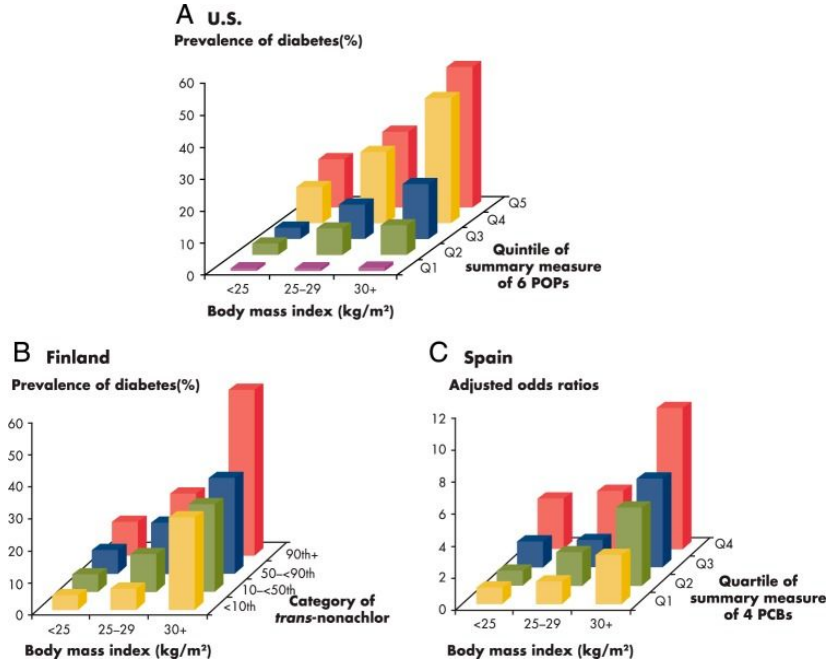
There is **no** relationship between BMI and diabetes risk in those in the bottom 10% of toxin load!

Barnes, A. S. (2011). The epidemic of obesity and diabetes.

Lee D.-H., et al. (2006). A strong dose-response relation between serum concentrations of persistent organic pollutants and diabetes: Results from the National Health and Examination Survey 1999-2002.

Toxins, not just obesity

Interaction between body mass index (BMI) and persistent organic pollutants (POPs) estimating the prevalence of T2D.

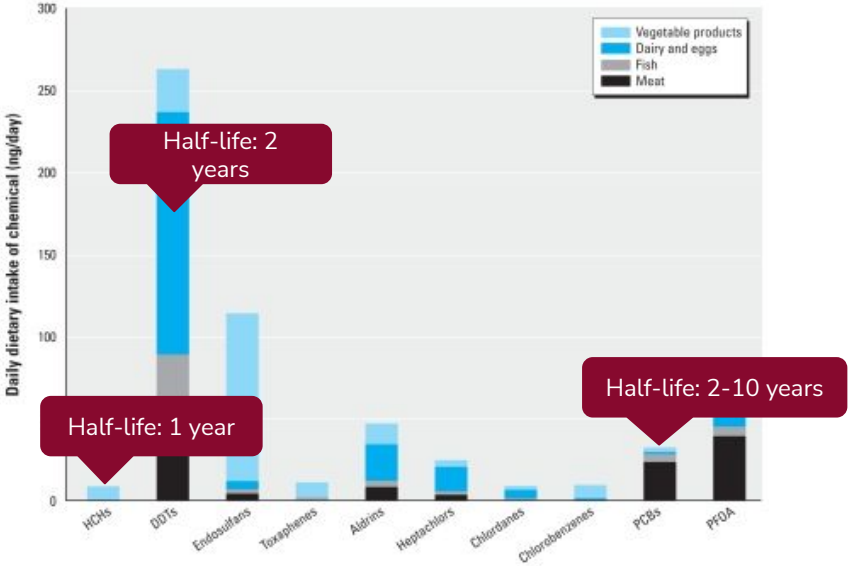


Lee, D.-H., et al. (2014). Chlorinated persistent organic pollutants, obesity, and type 2 diabetes.

Bioaccumulation of environmental toxins

Daily toxin exposure

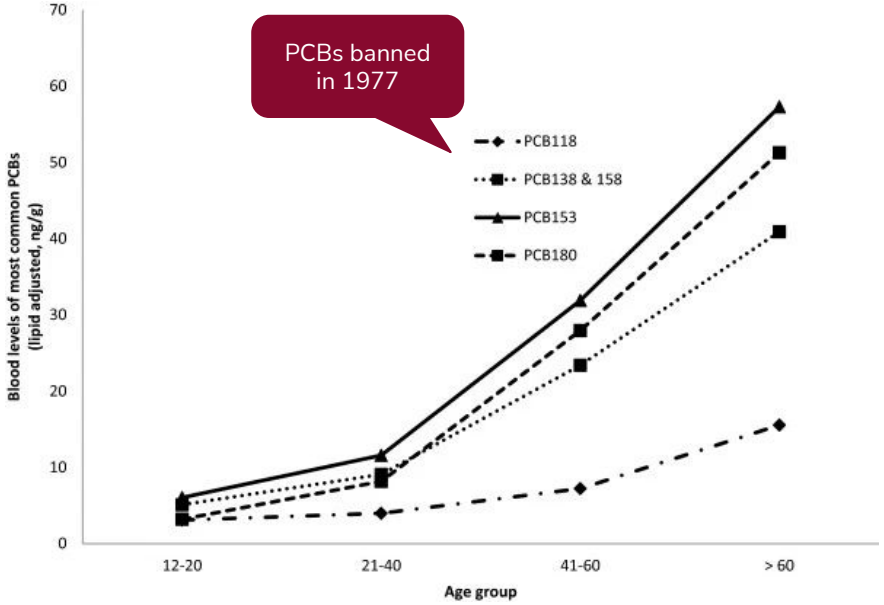
Estimation of per capita dietary exposure to pesticides, polychlorinated biphenyls (PCBs), and perfluorooctanoic acid (PFOA) using 2007 USDA food availability data, all ages, estimating values below the limit of detection as zero.



[Schecter, A., et al. (2010). Perfluorinated compounds, polychlorinated biphenyls, and organochlorine pesticide contamination in composite food samples from Dallas, Texas, USA.]

Persistent organic pollutants (POPs)

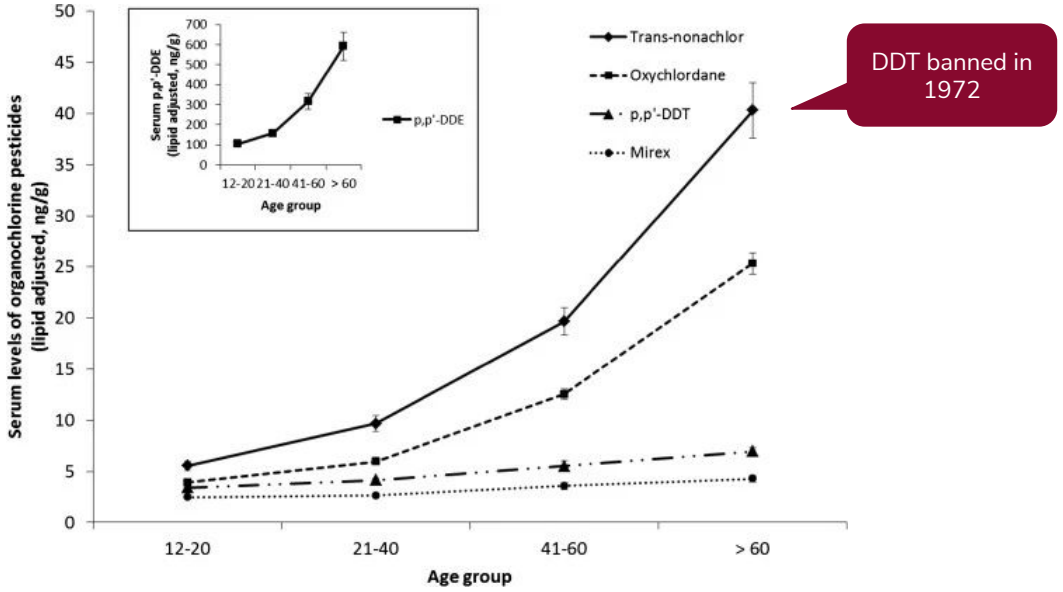
Blood levels of most common PCBs (lipid adjusted) in the general population by age group (NHANES 2003-2004).



Serdar, B., et al. (2014). 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.

Persistent organic pollutants (POPs)

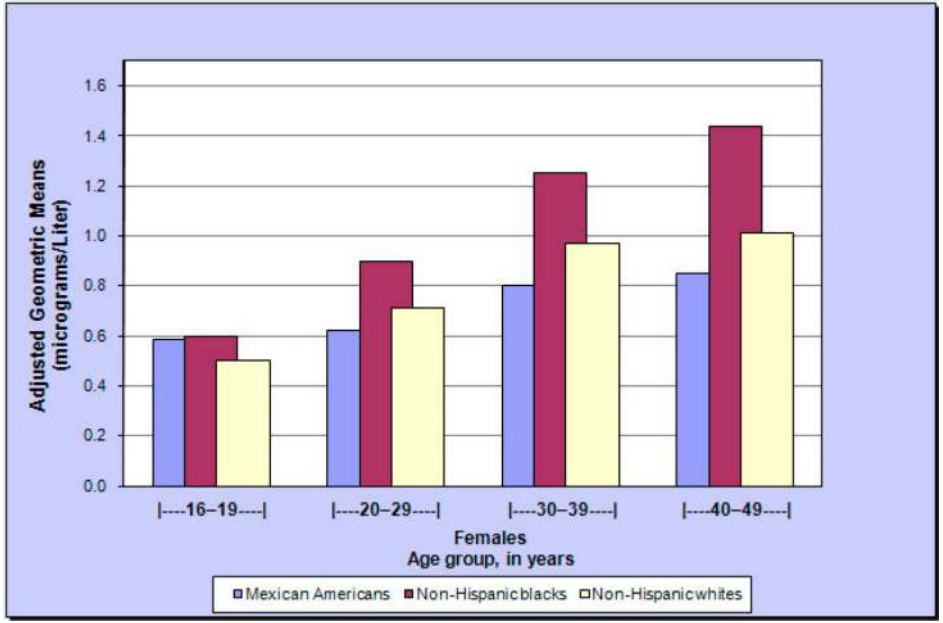
Blood levels of organochlorine pesticides (lipid adjusted) in the general population by age group (NHANES 2003-2004).



Serdar, B., et al. (2014). 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.

Mercury

Age-related changes in total blood mercury levels for females aged 16-49 by race/ethnicity, 1999-2006.



Centers for Disease Control and Prevention. (2009). Fourth national report on human exposure to environmental chemicals.

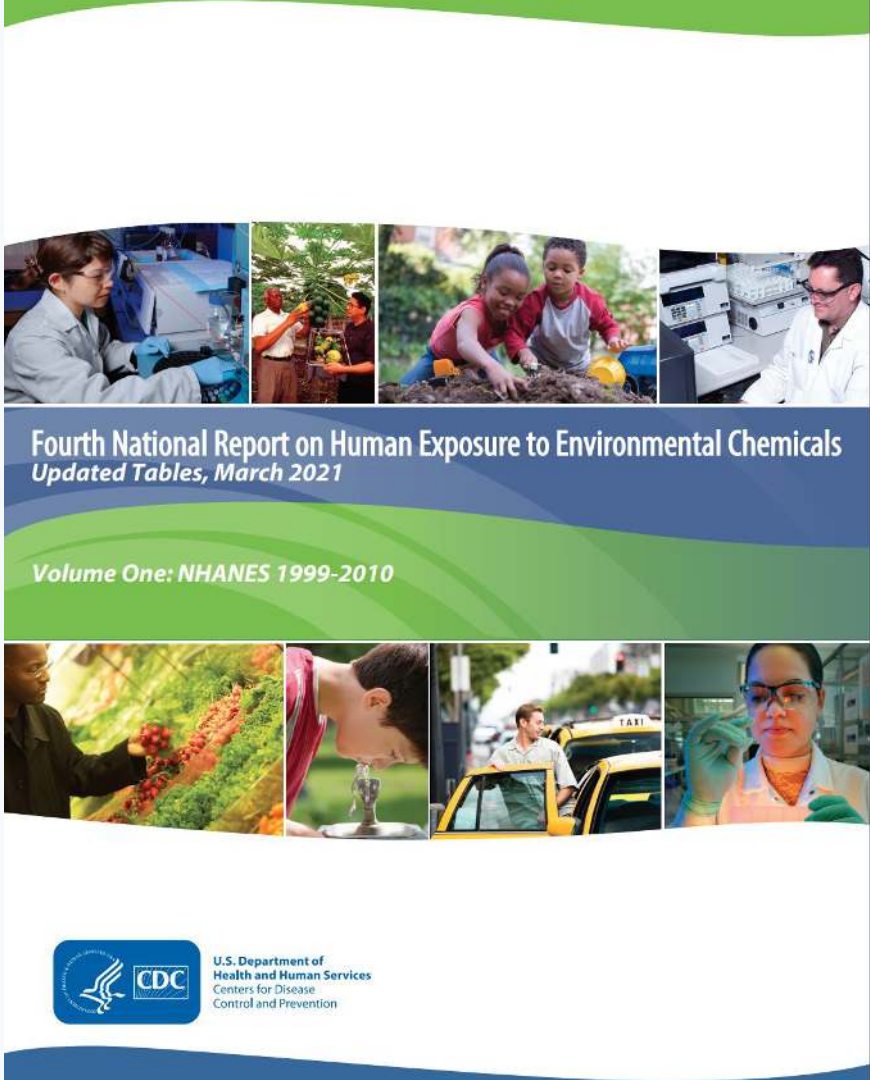
Substance priority list

2019 rank	Substance
1	Arsenic
2	Lead
3	Mercury
4	Vinyl chloride
5	Polychlorinated biphenyls
6	Benzene
7	Cadmium
8	Benzo(a)pyrene
9	Polycyclic aromatic hydrocarbons
10	Benzo(b)fluoranthene

Agency for Toxic Substances and Disease Registry. (2019). ATSDR's Substance Priority List.

Source of population toxicant load

Centers for Disease Control and Prevention
[Fourth national report on human exposure to environmental chemicals: Updated tables, March 2021.]

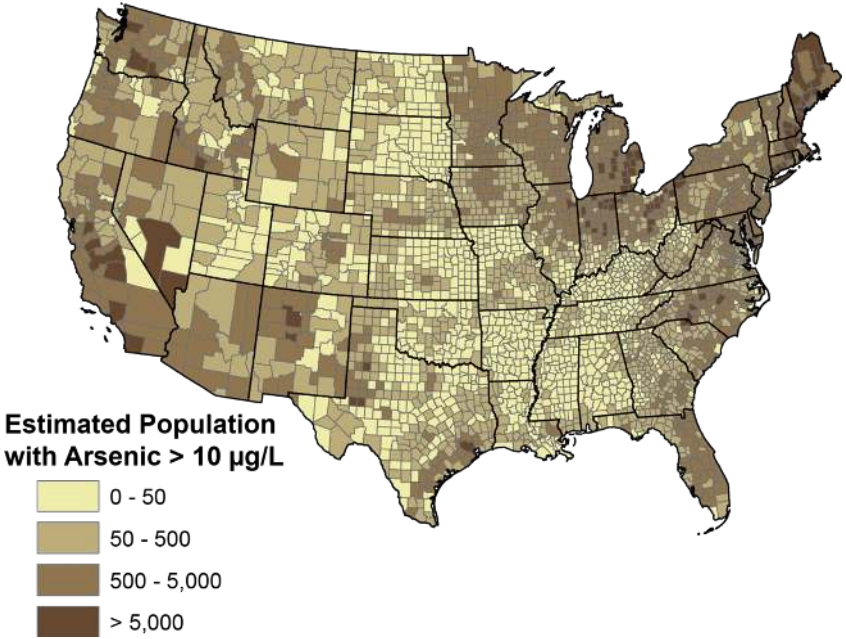


The five worst toxins:

Arsenic

Arsenic: well water contamination

Estimated population of private domestic well users with arsenic greater than 10 micrograms per liter.



It's estimated that **2.1 million** Americans may be drinking well water high in arsenic.

U.S. Geological Survey. (n.d.). Arsenic and drinking water.

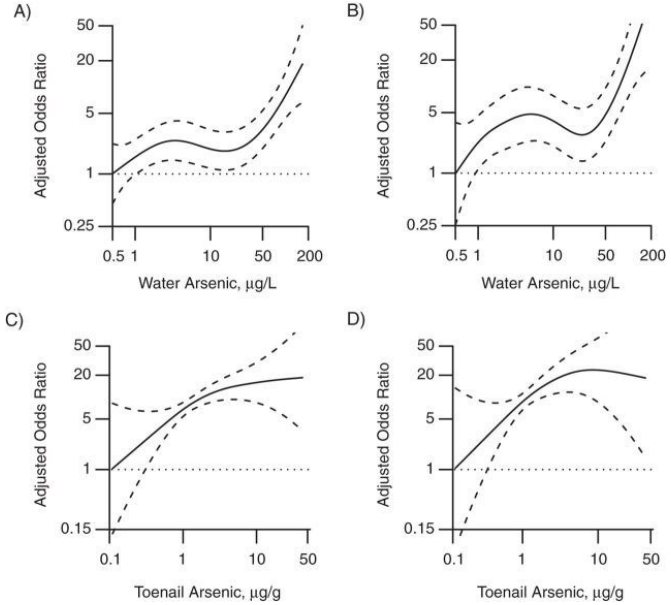
Arsenic: correlation with type 2 diabetes

Dose-response curve between arsenic exposure and change in risk of type 2 diabetes mellitus among residents exposed to arsenic in drinking water at levels less than 170 µg/L.

How As causes diabetes:

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

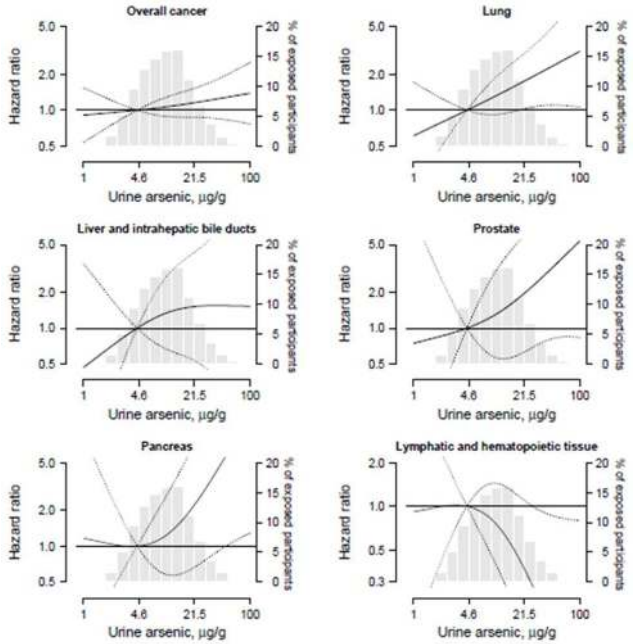
Toenail arsenic is the best measure for historic exposure.



[Pan, W.-C., et al. (2013). Association of low to moderate levels of arsenic exposure with risk of type 2 diabetes in Bangladesh.]

Arsenic: correlation with many cancers

Hazard ratios for cancer mortality by urine arsenic concentrations.

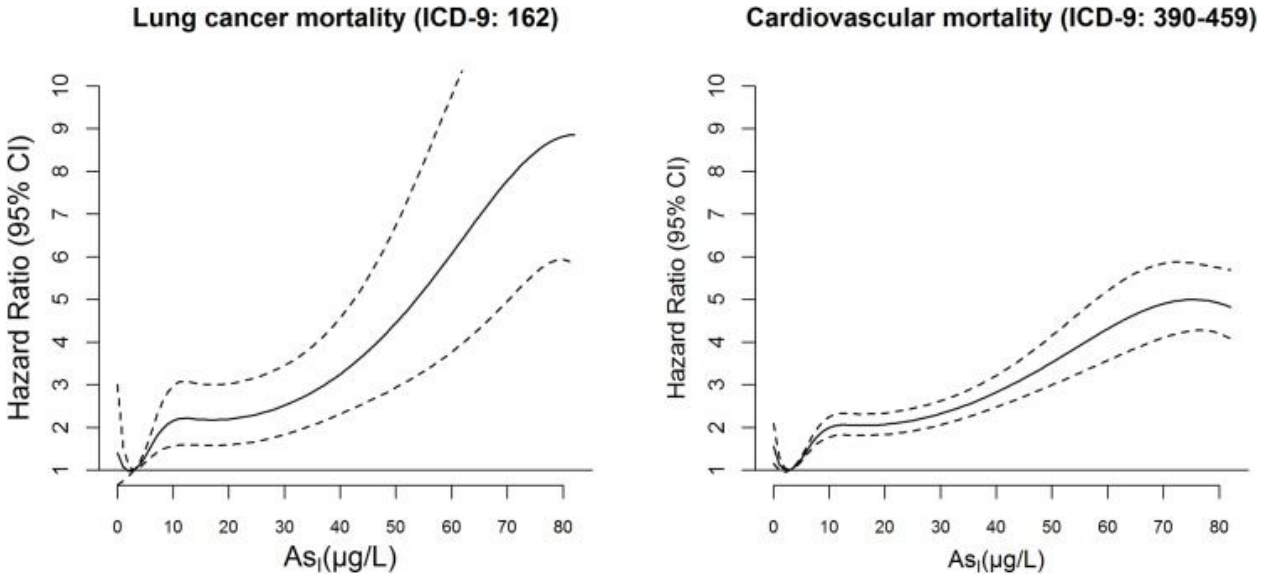


- Dose-dependent carcinogen
- 3,932 indigenous Americans
- Arsenic not associated with cancers of esophagus, stomach, colon, rectum, and breast
- Protective for blood cancers?
- Adjusted for age, sex, smoking status, BMI (kg/m^2)

[Pan, W.-C., et al. (2013). Association of low to moderate levels of arsenic exposure with risk of type 2 diabetes in Bangladesh.]

Arsenic: chronic disease mortality risk

Dose-response relationship between lifetime average arsenic concentrations at the individual level (As_I) and mortality risk for lung cancer and cardiovascular diseases in the study subjects, 1990–2010.



D'Ippoliti, D., et al. (2015). Arsenic in drinking water and mortality for cancer and chronic diseases in central Italy, 1990-2010.

Arsenic: urine concentrations

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the total U.S. population from the National Health and Nutrition Examination Survey.

Survey years	Geometric mean (95% CI)	50th Percentile (95% CI)	75th Percentile (95% CI)	90th Percentile (95% CI)	95th Percentile (95% CI)	Sample size
2003-04	8.30 (7.19-9.57)	7.70 (6.90-8.90)	16.0 (14.1-18.7)	37.4 (31.6-43.5)	65.4 (48.7-83.3)	2557
2005-06	9.29 (8.05-10.7)	8.65 (7.48-9.99)	17.1 (14.9-20.6)	41.1 (33.3-49.7)	66.7 (53.7-87.0)	2576
2007-08	8.10 (7.44-8.83)	7.49 (6.90-8.12)	14.9 (13.2-17.0)	33.3 (29.8-38.7)	50.8 (42.3-65.1)	2605
2009-10	9.28 (8.47-10.2)	8.15 (7.20-8.98)	18.0 (15.3-20.8)	44.6 (39.0-55.1)	85.6 (64.7-114)	2860

Centers for Disease Control and Prevention. (2021). Fourth national report on human exposure to environmental chemicals: Updated tables, March 2021.

Arsenic: common forms and sources

Toxicity of common forms of arsenic in humans.

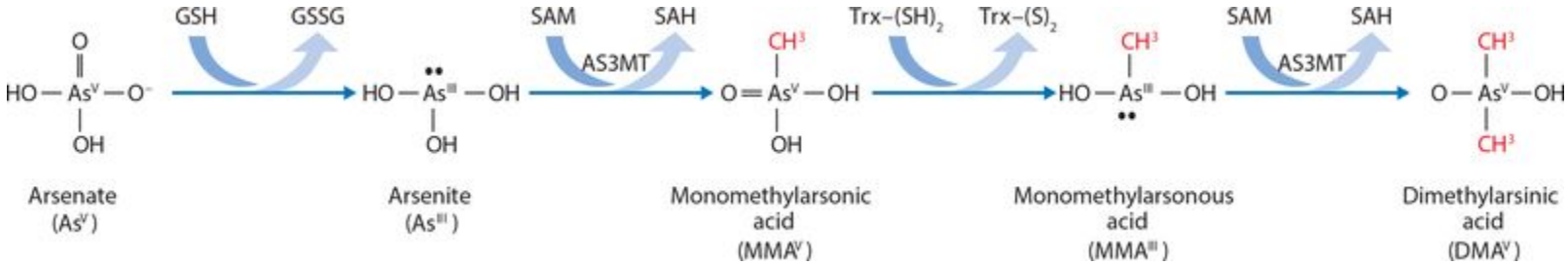
Species	Type	Half life	Primary source	LD50
MMA	Organic	10-20 hours	Food	2 mg/kg
Arsenate (V)	Inorganic	2-4 days	Water	8 mg/kg
Arsenite (III)	Inorganic	2-4 days	Water	26 mg/kg
DMA	Organic	10-20 hours	Food	648 mg/kg
Arsenobetaine	Organic	4-6 hours	Seafood	>4,000 mg/kg

- Primary dietary sources:
  - Chicken
  - Rice
  - Water
- The arsenic threshold for increased disease risk is **10.0 µg/L urine**.
- **>35%** of the U.S. population exceeds this threshold.

D'Ippoliti, D., et al. (2015). Arsenic in drinking water and mortality for cancer and chronic diseases in central Italy, 1990-2010.

Arsenic: metabolism

Multiple enzymes are involved in arsenic metabolism.

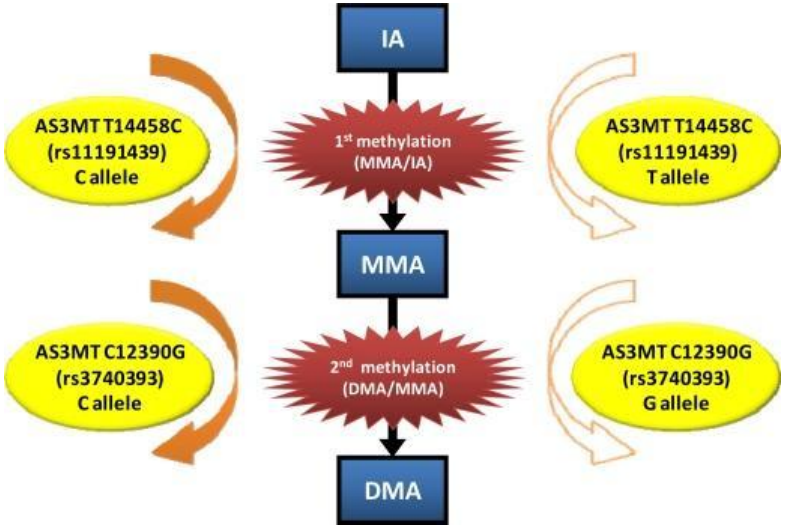


- MMA is **eight times more toxic** than inorganic arsenic.
- DMA is **400 times less toxic** than inorganic arsenic.
- Blood glutathione (GSH) has an inverse relationship with arsenic in urine and blood.

Bozack, A. K., et al. (2018). Nutritional influences on one-carbon metabolism: Effects on arsenic methylation and toxicity.

Arsenic: genetic impact on metabolism

Suspected universal AS3MT genotype-dependent methylation of arsenic.



- 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 ↑ As toxicity

- 1% of population

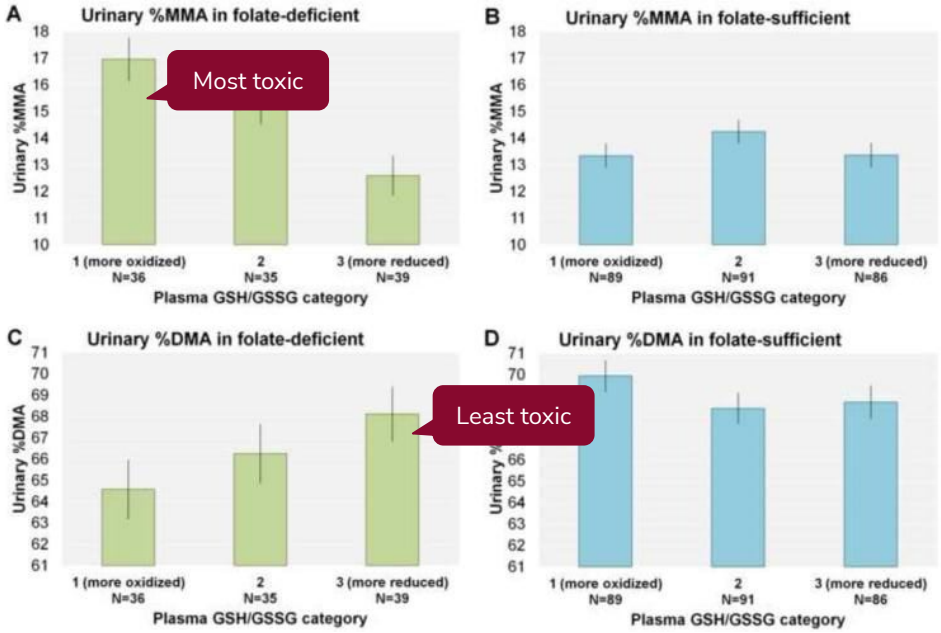
rs11191439 prevalence

- CC: 0.013
- CT: 0.181
- TT: 0.805

[Agusa, T., et al. (2011). Individual variations in inorganic arsenic metabolism associated with *AS3MT* genetic polymorphisms.]

Arsenic

Reduced glutathione is especially important when folate deficient.



[Niedzwiecki, M. M., et al. (2014). Interaction of plasma glutathione redox and folate deficiency on arsenic methylation capacity in Bangladeshi adults.]

Arsenic: % of disease due to arsenic

Disease	Threshold	% above threshold	Odds ratio	% of disease
Gout	12.5 µg/L	25%	5.5	52%
Cancer, prostate	13.3 µg/L	20%	3.3	32%
Cancer, pancreatic	13.3 µg/L	20%	2.5	23%
Diabetes	16.5 µg/L	20%	2.1	18%
Cancer, bladder	10.0 µg/L	10%	2.7	14%

García-Esquinas, E., et al. (2013). Arsenic exposure and cancer mortality in a US-based prospective cohort: the strong heart study.

Kuo, C. C., et al. (2014). Arsenic exposure, hyperuricemia, and gout in US adults.

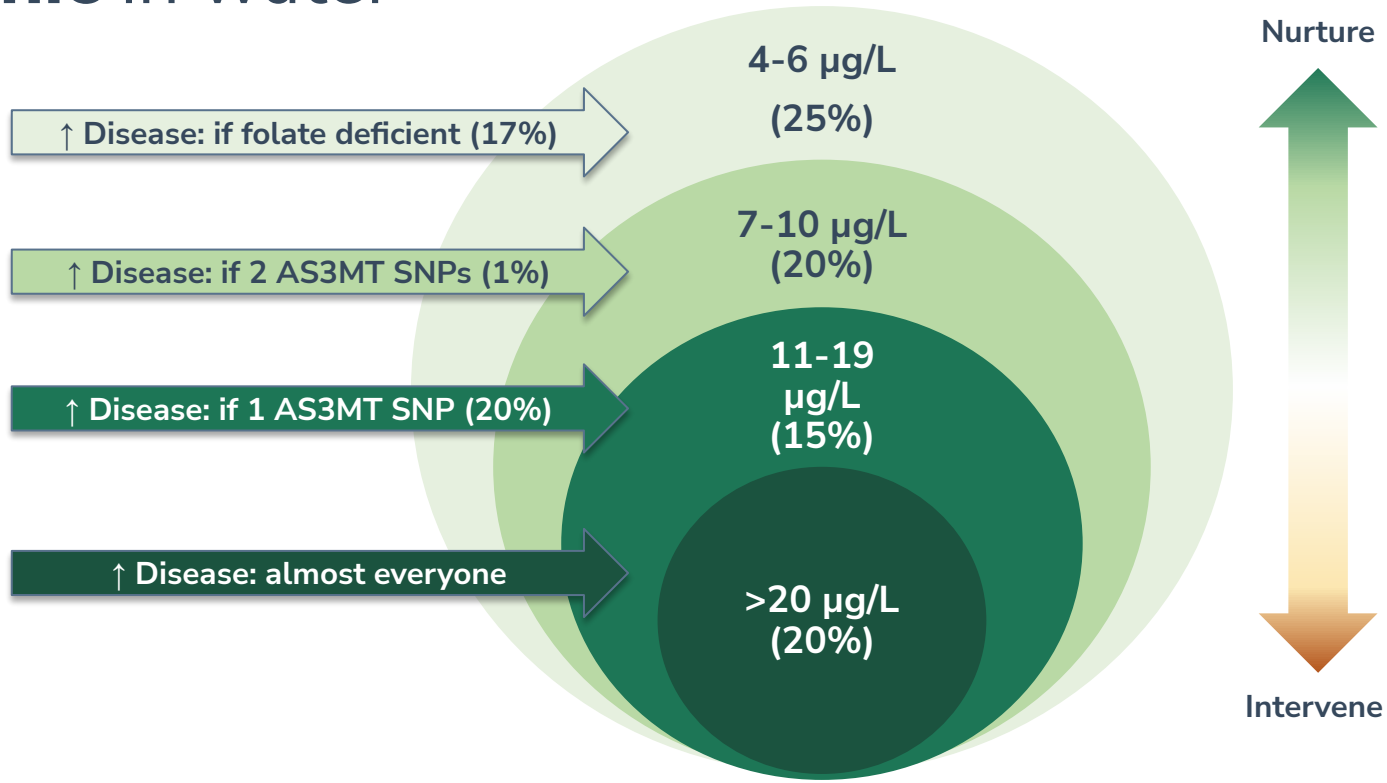
Navas-Acien, A., et al. (2008). Arsenic exposure and prevalence of type 2 diabetes in US adults.

Saint-Jacques, N, et al. (2014). Arsenic in drinking water and urinary tract cancers: a systematic review of 30 years of epidemiological evidence.

Arsenic: assessment

- If in normal environment, first morning urine
  - **<7.0 ug** arsenic/g creatinine
- If not in normal environment, toenails indicate historic exposure
  - **<0.5 ug/g**

Arsenic in water



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

Arsenic: assessment

- Arsenic in water **>20.0 µg/L** is toxic for everyone.
  (2% of reported U.S. public water supplies, higher in private wells).
- Arsenic in water **>10.0 µg/L** is toxic for everyone, if also another exposure such as regularly eating chicken or rice.
  (10% of reported US public water supplies, higher in private wells).
- If 1 of 2 AS3MT SNPs, toxic effects **>11.0 µg/L** of water or significant other Arsenic sources (regularly eating rice or chicken).
- If both AS3MT SNPs, toxic effects **>7.0 µg/L** or significant other Arsenic.
  - Incidence of the SNPs are 8% and 14% ⇒
    - 21% experience toxicity from Arsenic levels lower than “safe.”
    - 1% likely suffer arsenic toxicity if regularly eating rice and chicken, even if water arsenic not high. Deadly if also Arsenic in water.

Arsenic: intervention

- **B-vitamin** supplementation if elevated homocysteine.
- **Glutathione** support.
- Treat water if above **5.0 µg/L**.

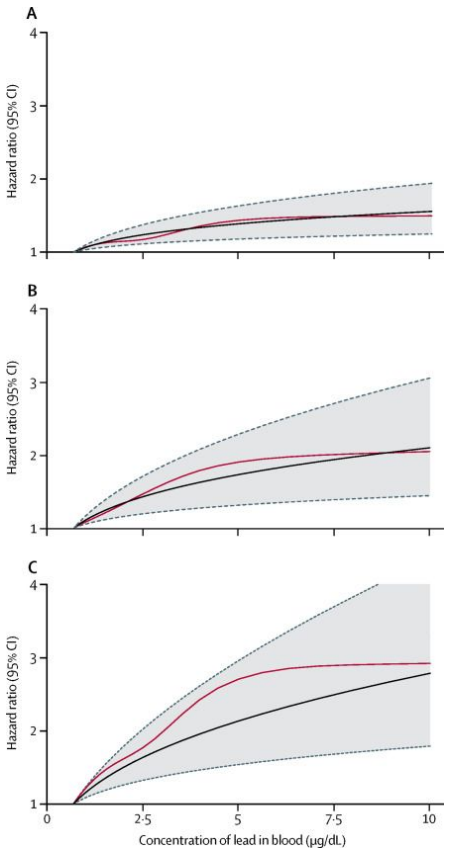
The five worst toxins:

Lead

Lead: mortality risk

Dose-response curves for concentrations of lead in blood and mortality.

Curve		Population attributable fraction (95% CI)
A	All-cause mortality	18.0% (10.9-26.1)
B	Cardiovascular disease mortality	28.7% (15.5-39.5)
C	Ischaemic heart disease mortality	37.4% (23.4-48.6)



[Lanphear, B. P., et al. (2018). Low-level lead exposure and mortality in US adults: a population-based cohort study.]

Lead: % of disease due to lead

Disease	Threshold	% above threshold	Odds ratio	% of disease
Ischemic death	5.0 ug/dL	20%	6.3	37%
Infertility, male	0.8 ug/dL	33%	N/A	↓ fertility 27%
All-cause mortality	2.0 ug/dL	67%	1.4	18%
ALS	2.4 ug/dL bld	33%	1.8	6%
ADHD	2.3 ug/dL	1.3%	2.5	2%
Juvenile IQ	5-10 ug/dL	~5%	N/A	↓ 5 points

Buck Louis, G. M., et al. (2012). Heavy metals and couple fecundity, the LIFE Study.

Lanphear, B. P., et al. (2018). Low-level lead exposure and mortality in US adults: a population-based cohort study.

Mazumdar, M., et al. (2011). Low-level environmental lead exposure in childhood and adult intellectual function: a follow-up study.

Park, J. H., et al. (2016). Blood lead concentrations and attention deficit hyperactivity disorder in Korean children: a hospital-based case control study.

Wang, M.-D., et al. (2014). A meta-analysis of observational studies of the association between chronic occupational exposure to lead and amyotrophic lateral sclerosis.

Lead: blood concentrations

Geometric mean and selected percentiles of blood concentrations (in µg/L) for the total U.S. population from the National Health and Nutrition Examination Survey.

Survey years	Geometric mean (95% CI)	50th Percentile (95% CI)	75th Percentile (95% CI)	90th Percentile (95% CI)	95th Percentile (95% CI)	Sample size
1999-00	1.66 (1.60-1.72)	1.60 (1.60-1.70)	2.50 (2.40-2.60)	3.80 (3.60-4.00)	5.00 (4.70-5.50)	7970
2001-02	1.45 (1.39-1.51)	1.40 (1.40-1.50)	2.20 (2.10-2.30)	3.40 (3.20-3.60)	4.50 (4.20-4.70)	8945
2003-04	1.43 (1.36-1.50)	1.40 (1.30-1.50)	2.10 (2.10-2.20)	3.20 (3.10-3.30)	4.20 (3.90-4.40)	8373
2005-06	1.29 (1.23-1.36)	1.27 (1.20-1.34)	2.01 (1.91-2.11)	3.05 (2.86-3.22)	3.91 (3.64-4.18)	8407
2007-08	1.27 (1.21-1.34)	1.22 (1.18-1.30)	1.90 (1.80-2.00)	2.80 (2.67-2.96)	3.70 (3.50-3.90)	8266
2009-10	1.12 (1.08-1.16)	1.07 (1.03-1.12)	1.70 (1.62-1.77)	2.58 (2.45-2.71)	3.34 (3.14-3.57)	8793

Centers for Disease Control and Prevention. (2021). Fourth national report on human exposure to environmental chemicals: Updated tables, March 2021.

Lead: common sources

- Primary sources:
  - Bone loss
  - Dust
  - Lead-containing dishes
  - Maternal–fetal exchange
  - Water
- The lead threshold is **1.0 ug/dL of blood** (no safe level of Pb)
- **>80%** of the U.S. population exceeds this threshold.

Lanphear, B. P., et al. (2018). Low-level lead exposure and mortality in US adults: a population-based cohort study.

Lead: assessment

- Blood lead
  - Children: **<3.0 ug/dL**
  - Adults: **<5.0 ug/dL**

Lead: intervention

General

- Maintain bone health.
- If home was built or water supply was installed before 1987, test water in home.

Supplements

- Calcium: 500 bid
- Vitamin C: 500 bid
- NAC: 500 mg bid

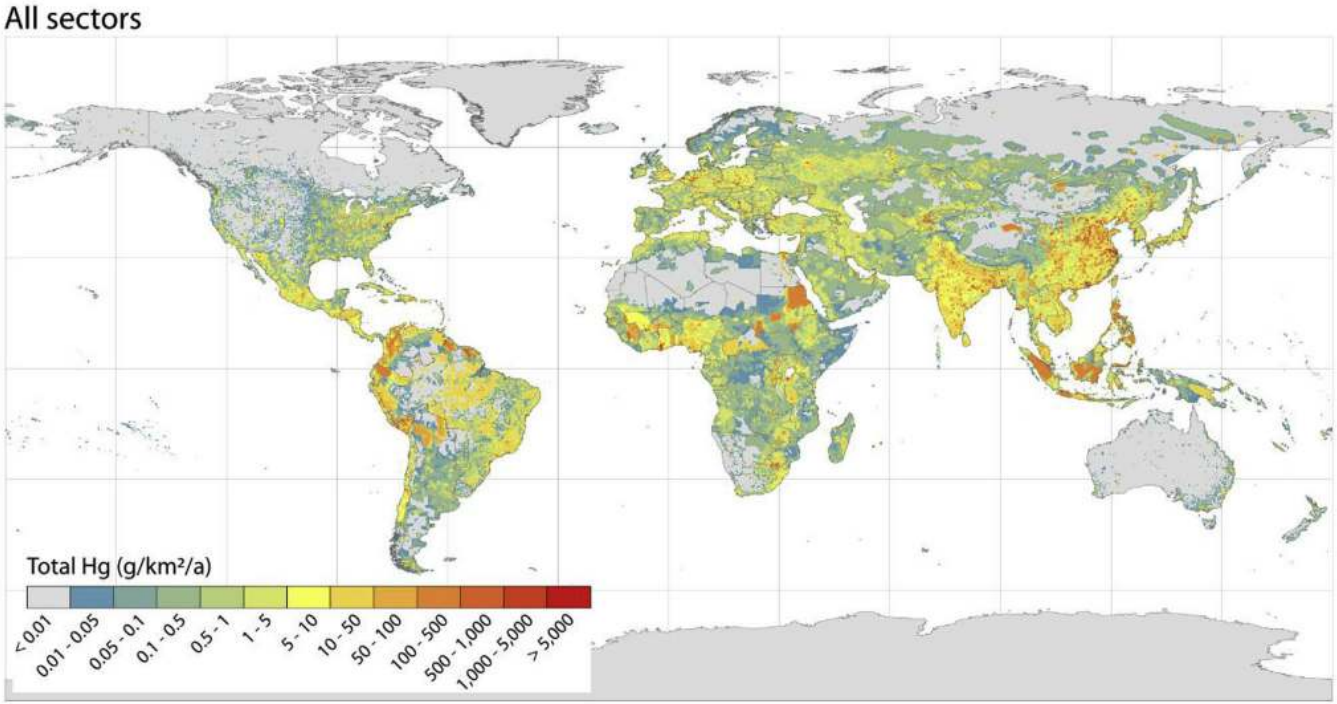
If patient has symptoms and high blood levels of lead:

- EDTA: oral, IV (physician protocol)
- DMSA: oral, 250 mg every 3 days

The five worst toxins:

Mercury

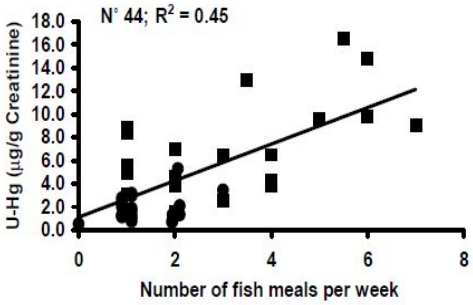
Mercury: worldwide emissions

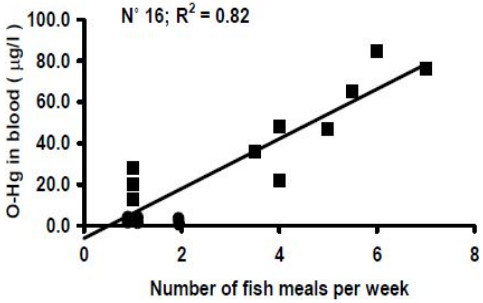


U.S. Environmental Protection Agency. (n.d.). Mercury emissions: The global context.

Mercury: correlation with fish consumption

Urinary and blood mercury levels and weekly fish consumption.





- Total Hg urinary excretion is proportional to amount of fish eaten.
- Impaired psychomotor performance:
  - R = 0.38 blood
  - R = 0.77 urine
- There is a large variation in the amount of Hg in fish.

Apostoli, P., et al. (2002). Assessment of reference values for mercury in urine: the results of an Italian polycentric study.

Carta, P., et al. (2003). Sub-clinical neurobehavioral abnormalities associated with low level of mercury exposure through fish consumption.

Mercury: levels in seafood

Best Choices
EAT 2 TO 3 SERVINGS A WEEK

- Anchovy
- Atlantic croaker
- Atlantic mackerel
- Black sea bass
- Butterfish
- Catfish
- Clam
- Cod
- Crab
- Crawfish
- Flounder
- Haddock
- Hake
- Herring
- Lobster, American and spiny
- Mullet
- Oyster
- Pacific chub mackerel
- Perch, freshwater and ocean
- Pickerel
- Plaice
- Pollock
- Salmon
- Sardine
- Scallop
- Shad
- Shrimp
- Skate
- Smelt
- Sole
- Squid
- Tilapia
- Trout, freshwater
- Tuna, canned light (includes skipjack)
- Whitefish
- Whiting

OR

Good Choices
EAT 1 SERVING A WEEK

- Bluefish
- Buffalofish
- Carp
- Chilean sea bass/ Patagonian toothfish
- Grouper
- Halibut
- Mahi mahi/ dolphinfish
- Monkfish
- Rockfish
- Sablefish
- Sheepshead
- Snapper
- Spanish mackerel
- Striped bass (ocean)
- Tilefish (Atlantic Ocean)
- Tuna, albacore/ white tuna, canned and fresh/frozen
- Tuna, yellowfin
- Weakfish/ seatrout
- White croaker/ Pacific croaker

Choices to Avoid
HIGHEST MERCURY LEVELS

- King mackerel
- Marlin
- Orange roughy
- Shark
- Swordfish
- Tilefish (Gulf of Mexico)
- Tuna, bigeye

* Some fish caught by family and friends, such as larger carp, catfish, trout and perch, are more likely to have fish advisories due to mercury or other contaminants. State advisories will tell you how often you can safely eat those fish.

www.FDA.gov/fishadvice
www.EPA.gov/fishadvice

EPA United States Environmental Protection Agency

FDA U.S. FOOD & DRUG ADMINISTRATION

LEAST MERCURY

- Anchovies
- Butterfish
- Catfish
- Clam
- Crab (Domestic)
- Crawfish/Crayfish
- Croaker (Atlantic)
- Flounder*
- Haddock (Atlantic)*
- Hake
- Herring
- Mackerel (N. Atlantic, Chub)
- Mullet
- Oyster
- Perch (Ocean)
- Plaice
- Pollock
- Salmon (Canned)**
- Salmon (Fresh)**
- Sardine
- Scallop*
- Shad (American)
- Shrimp*
- Sole (Pacific)
- Squid (Calamari)
- Tilapia
- Trout (Freshwater)
- Whitefish
- Whiting

MODERATE MERCURY

EAT SIX SERVINGS OR LESS PER MONTH:

- Bass (Striped, Black)
- Carp
- Cod (Alaskan)
- Croaker (White Pacific)
- Halibut (Atlantic)*
- Halibut (Pacific)
- Jacksmelt (Silverside)
- Lobster
- Mahi Mahi
- Monkfish*
- Perch (Freshwater)
- Sablefish
- Skate*
- Snapper*
- Tuna (Canned chunk light)
- Tuna (Skipjack)*
- Weakfish (Sea Trout)

HIGH MERCURY

EAT THREE SERVINGS OR LESS PER MONTH:

- Bluefish
- Grouper*
- Mackerel (Spanish, Gulf)
- Sea Bass (Chilean)*
- Tuna (Canned Albacore)
- Tuna (Yellowfin)*

HIGHEST MERCURY

AVOID EATING:

- Mackerel (King)
- Marlin*
- Orange Roughy*
- Shark*
- Swordfish*
- Tilefish*
- Tuna (Bigeye, Ahi)*

***Fish in Trouble!** These fish are perilously low in numbers or are caught using environmentally destructive methods.

**** Farmed salmon** may contain PCB's, chemicals with serious long-term health effects.

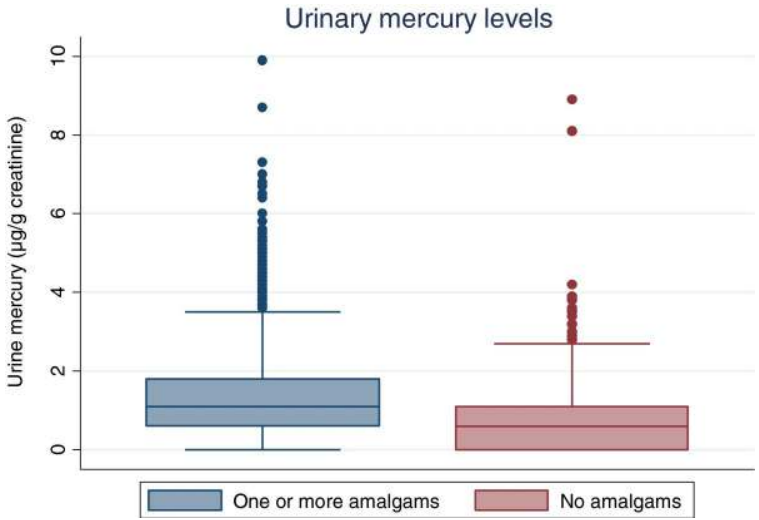
Information in this guide is based on averages from the FDA's test results for mercury in fish and the EPA's determination of safe levels of mercury for women of reproductive age. Some individual fish have mercury concentrations significantly higher than the average. For more details, see: www.nrdc.org/mercury.

[Natural Resources Defense Council. (2006). Mercury in fish.]

[U.S. Food & Drug Administration. (2020). Advice about eating fish.]

Mercury: dental amalgams

Frequencies of urine mercury levels in those with and without amalgams.



- A typical amalgam is **55% Hg.**
  - = 400 mg per filling
- One amalgam will release **1 ug/d.**
- Average older adult has 10 fillings
- Hg excretion is proportional to surface area (poorer correlation with count).
  - Consider the **amalgam area**, not the number of amalgams.
- Amalgams release elemental Hg.
  - Hg is methylated by gut bacteria and absorbed.

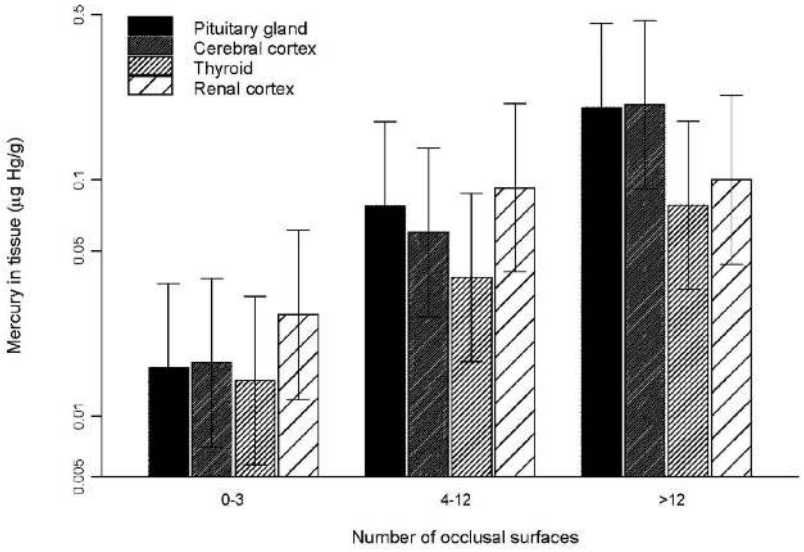
Apostoli, P., et al. (2002). Assessment of reference values for mercury in urine: the results of an Italian polycentric study.

Dutton, D. J., et al. (2013). The association between amalgam dental surfaces and urinary mercury levels in a sample of Albertans, a prevalence study.

Lorscheider, F. L., et al. (1995). Mercury exposure from “silver” tooth fillings: emerging evidence questions a traditional dental paradigm.

Mercury: dental amalgams

Total mercury levels by anatomic site and number of occlusal amalgam surfaces (geometric means and 95% CI).

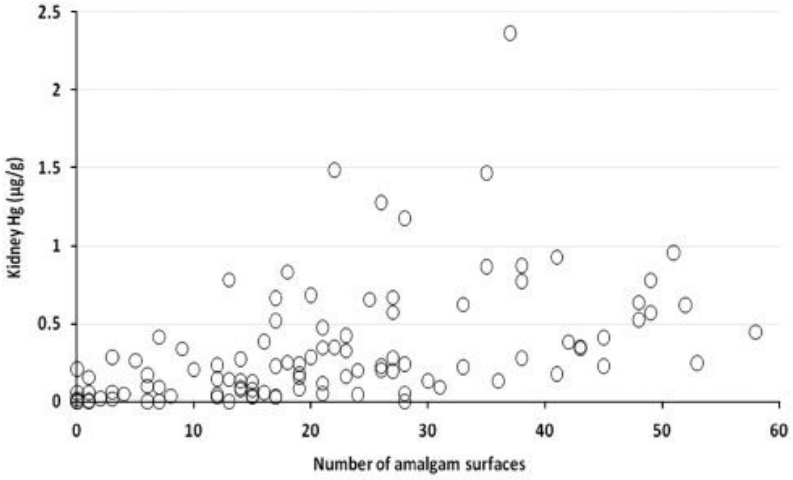


Guzzi, G., et al. (2006). Dental amalgam and mercury levels in autopsy tissues: Food for thought.

Mercury: what live tissues tell us about amalgams

Dose-response curve between arsenic exposure and change in risk of type 2 diabetes mellitus among residents exposed to arsenic in drinking water at levels less than 170 µg/L.

- Donated kidneys for transplant
- R = 0.62 correlation with number of amalgam surfaces
- **6% increase** in kidney Hg per amalgam surface



Barregard, L., et al. (2010). Cadmium, mercury, and lead in kidney cortex of living kidney donors: Impact of different exposure sources.

Mercury in natural health products

Natural health products (herbal medicine) must be considered.

Element	Results (ug/g) in Chinese herbal medicine	Results (ug/g) in Ayurvedic herbal medicine
Aluminum	52	1,973
Arsenic	510	866
Copper	1.5	27
Lead	0.57	3.5
Mercury	1,200	5,000

Steven Mouratidis, ND, Melbourne. Analysis performed by Inductively Coupled Plasma - Mass Spectrometry (ICP-MS).

Mercury: human release into the environment

Global anthropogenic emissions of Hg in 2000 (in ton).

Continent	Stationary combustion
Africa	205.2
Asia (excl. Russia)	878.7
Australasia	112.6
Europe (excl. Russia)	88.8
Russia	26.5
South America	31.0
North America	79.6
Total	1422.4

>50% of global Hg comes from China

Pacyna, E. G., et al. (2006). Global anthropogenic mercury emission inventory for 2000.

Mercury: % of disease due to mercury

Disease	Threshold	% above threshold	Odds ratio	% of disease
Hashimoto's disease	.8 µg/L bld	20%	2.2	20.0%
ADHD	~3.5ug/dL maternal blood	~8-9%	1.6	Big error range 3%
Infertility, female	Quartile	25%	1.04	1%

Burch, J. B., et al. (2014). Mercury in fish and adverse reproductive outcomes: results from South Carolina.

Gallagher, C. M., et al. (2012). Mercury and thyroid autoantibodies in U.S. women, NHANES 2007-2008.

Yoshimasu, K., et al. (2014). A meta-analysis of the evidence on the impact of prenatal and early infancy exposures to mercury on autism and attention deficit/hyperactivity disorder in the childhood.

Mercury: blood concentrations

Geometric mean and selected percentiles of blood concentrations (in µg/L) for the total U.S. population from the National Health and Nutrition Examination Survey.

Survey years	Geometric mean (95% CI)	50th Percentile (95% CI)	75th Percentile (95% CI)	90th Percentile (95% CI)	95th Percentile (95% CI)	Sample size
2003-04	.797 (.703-.903)	.800 (.700-.900)	1.70 (1.50-1.90)	3.30 (2.90-3.90)	4.90 (4.30-5.50)	8373
2005-06	.863 (.787-.946)	.830 (.760-.920)	1.66 (1.48-1.93)	3.20 (2.87-3.54)	4.64 (4.17-5.25)	8407
2007-08	.769 (.689-.859)	.740 (.660-.830)	1.48 (1.29-1.69)	2.95 (2.46-3.59)	4.64 (3.74-5.79)	8266
2009-10	.863 (.792-.941)	.790 (.730-.880)	1.68 (1.49-1.91)	3.43 (3.07-3.84)	5.13 (4.57-5.67)	8793

Centers for Disease Control and Prevention. (2021). Fourth national report on human exposure to environmental chemicals: Updated tables, March 2021.

Mercury: common sources

- Primary sources:
  - Dental amalgams
  - Fish
  - Shellfish
- **Methylmercury** is the most cardiotoxic (found in fish).
- There is no known safe level of Hg.
- 50% of the population has elevated concentrations.

Mercury: assessment

- Neurological symptoms almost always first indication
- Blood and urine indicate current exposure
  - Urine **<3.0 µg/g** (creatinine corrected)
- Hair indicates methylmercury exposure (usually primarily fish)

Mercury: intervention

Oral health

- If the patient has symptoms and amalgams, particularly with gold caps on amalgams or blue lines on gums, remove the amalgams with an **ecological dentist**.

Diet

- Only eat low-mercury fish.

Supplements

Increase mercury excretion:

- Fiber: at least 10g/d
- NAC: 500 mg bid
- Trace minerals
- DMSA: oral, 250 mg every 3 days

Protect against damage:

- Curcumin: 60 mg/d

The five worst toxins:

Bisphenols

Bisphenols: a troubled history

Bisphenol A (BPA) and diethylstilbestrol (DES) are two synthetic compounds.

BPA and DES

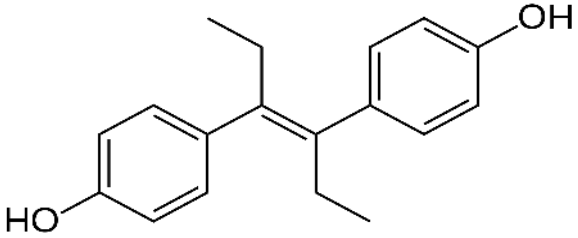
- Synthetic estrogens developed during the 1930s.
- Very similar chemical structures.
- So widely used; very difficult to avoid exposure.
- Technically non-persistent, but practically semi-persistent.

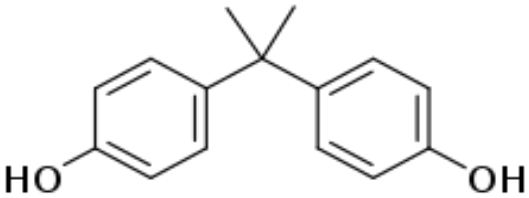
DES

- DES ‘won’ and was prescribed for pregnant women.
- Discontinued due to urogenital cancers in children and many other clinical problems.

BPA

- BPA was ‘put on the shelf’ until the 1950s, when its ability to harden plastics was discovered.





Bisphenols: diabetes risk

There are 211 PubMed hits for: bisphenols / diabetes / human.

Odd ratios (ORs) [95% confidence interval (CI)] for T2DM by log-transformed urinary concentrations of bisphenols in logistic regression analyses.

	Unadjusted		Multiple adjusted [a]	
	OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
BPAF [b]	4.70 (3.29, 6.71)	<0.001	4.95 (3.15, 7.79)	<0.001
BPS [b]	1.46 (1.22, 1.74)	<0.001	1.73 (1.37, 2.18)	<0.001
BPA [b]	0.85 (0.69, 1.05)	0.138	1.02 (0.78, 1.32)	0.897
∑BPs [b]	1.01 (0.75, 1.37)	0.936	1.28 (0.89, 1.85)	0.189

Note: BPAF, bisphenol AF; BPS, bisphenol S; BPA, bisphenol A; ∑BPs, the mass sum of eight bisphenol concentrations.

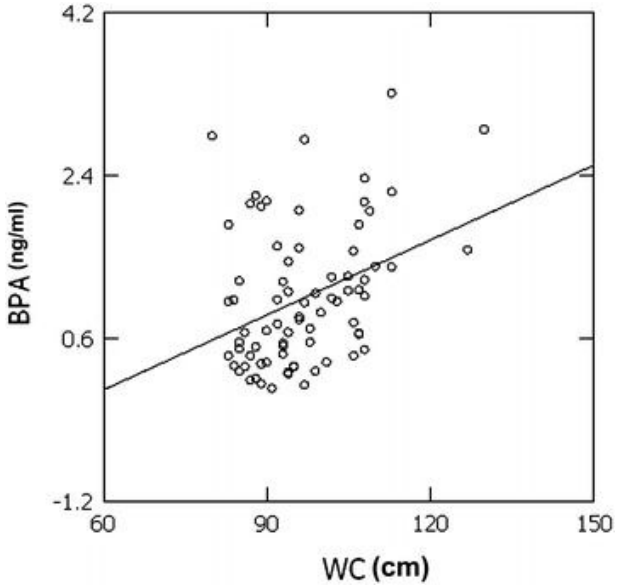
[a] Adjusted for sex, age, body mass index, urinary creatinine, smoking and alcohol-drinking status, exercising status, education level, family history of diabetes, and blood pressure.

[b] Variable was log-transformed.

Duan, Y., et al. (2018). Association of urinary concentrations of bisphenols with type 2 diabetes mellitus: A case-control study.

BPA: correlation with obesity

The correlation between bisphenol-A (BPA ng/ml) and waist circumference (WC cm) was analyzed by the robust regression.

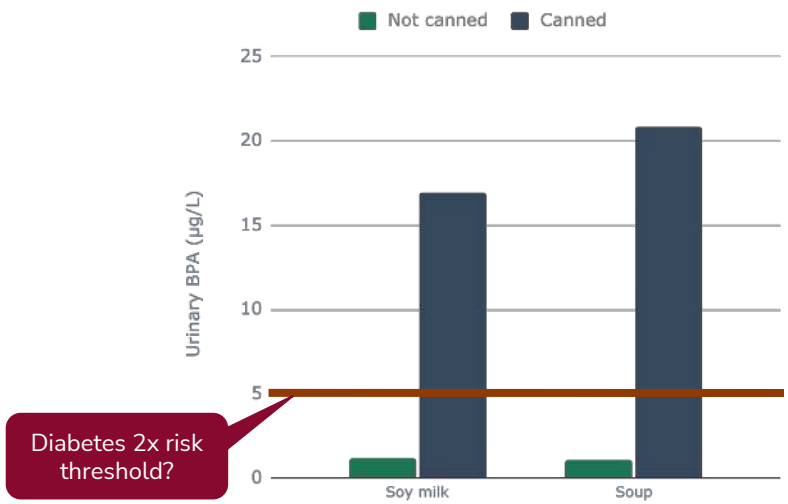


Savastano, S., et al. (2015). Bisphenol-A plasma levels are related to inflammatory markers, visceral obesity and insulin-resistance: a cross-sectional study on adult male population.

BPA in food packaging

Urinary bisphenol A concentration after soy milk and soup consumption.

- One 12 oz (355 mL) serving daily for one week of either fresh soup or canned lentil soup (Progresso).
  - **12-fold increase** in BPA
- Two servings of 6 oz (177 mL) soy milk in can compared to glass.
  - **16-fold increase** in BPA
  - Systolic BP elevated by **4.5 mm Hg**



Bae, S., et al. (2015). Exposure to bisphenol A from drinking canned beverages increases blood pressure: randomized crossover trial.

Carwile, J. L., et al. (2011). Canned soup consumption and urinary bisphenol A: A randomized crossover trial.

BPA alternatives?

Generally, BPA alternatives are not safer.

- Substitutes include:
  - Bisphenol F (BPF)
  - Bisphenol S (BPS)
  - Bisphenol Z (BPZ)
- They have very similar **endocrine-disrupting** effects.
- Considered **semi-persistent** because they are so prevalent in society.
- As BPA levels have gone down, other bisphenols have gone up in proportion.

Bisphenols: urinary concentrations

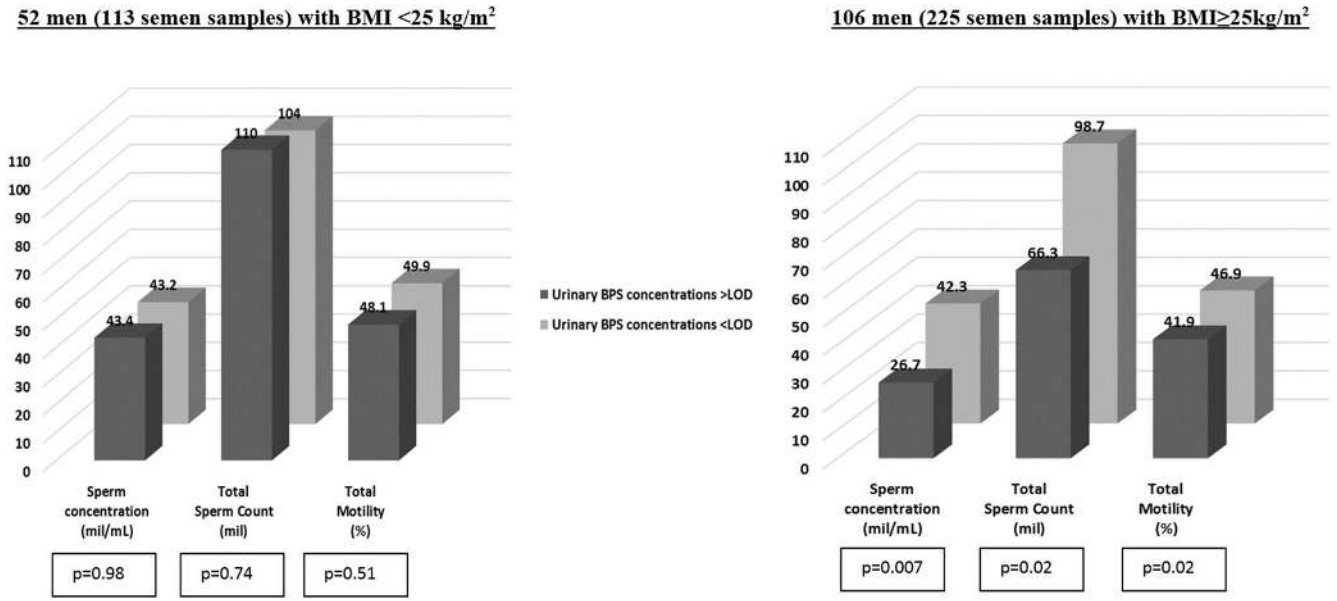
Geometric mean of urine concentrations (in µg/L) for the total U.S. population from the National Health and Nutrition Examination Survey.

Survey years	BPA geometric mean	BPF geometric mean	BPS geometric mean
2003-04	2.58	N/A	N/A
2013-14	1.28	0.53	0.43

Centers for Disease Control and Prevention. (2021). Fourth national report on human exposure to environmental chemicals: Updated tables, March 2021.

BPS decreases male fertility

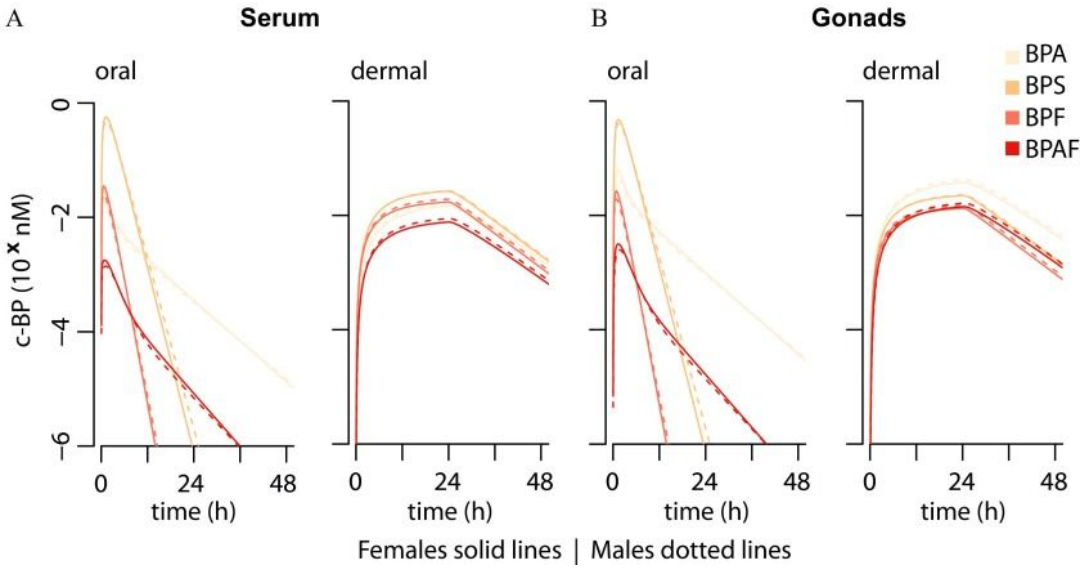
Harmful effects are seen primarily in overweight and obese men.



[Ghayda, R. A., et al. (2019). Urinary bisphenol S concentrations: Potential predictors of and associations with semen quality parameters among men attending a fertility center.]

Bisphenol half-lives

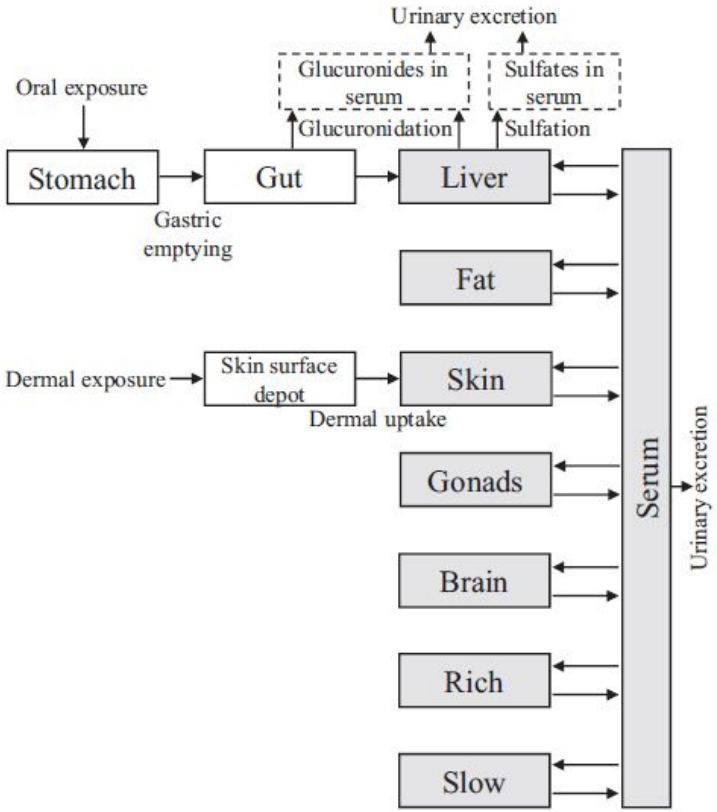
Modeled concentration profiles of unconjugated BPA, BPS, BPF, and BPAF obtained with the basic PBPK models in serum (A) and gonads (B) for adults (18–45 y)...



[Karrer, C. et al. (2018). Physiologically based pharmacokinetic (PBPK) modeling of the bisphenols BPA, BPS, BPF, and BPAF with new experimental metabolic parameters: Comparing the pharmacokinetic behavior of BPA with its substitutes.]

Bisphenol detoxification

- Bisphenols are non-persistent.
- Half lives range from 0.5 to 4.0 days.



[Karrer, C. et al. (2018). Physiologically based pharmacokinetic (PBPK) modeling of the bisphenols BPA, BPS, BPF, and BPAF with new experimental metabolic parameters: Comparing the pharmacokinetic behavior of BPA with its substitutes.]

BPA: % of disease due to BPA

Disease	Threshold	% above threshold	Odds ratio	% of disease
Diabetes	2.8 ug/L	28%	N/A	11%
Fetal abnormalities	N/A	N/A	N/A	Higher in fetuses with abnormalities
Infertility, male	44-94 pg/ml 98-205 69-228 84-330	N/A	N/A	Normospermic Oligospermic Teratospermic Azoospermic
IVF failure	Urine levels	N/A	Inversely proportional	# oocytes retrieved

Mok-Lin, E., et al. (2010). Urinary bisphenol A concentrations and ovarian response among women undergoing IVF.

Song, Y., et al. (2016). Endocrine-disrupting chemicals, risk of type 2 diabetes, and diabetes-related metabolic traits: A systematic review and meta-analysis.

Vitku, J., et al. Differences in bisphenol A and estrogen levels in the plasma and seminal plasma of men with different degrees of infertility.

Yamada, H., et al. (2002). Maternal serum and amniotic fluid bisphenol A concentrations in the early second trimester.

BPA: assessment

- Total bisphenols are preferred, but not commercially available.
- Urinary BPA
  - The lower the better!

Bisphenols: intervention

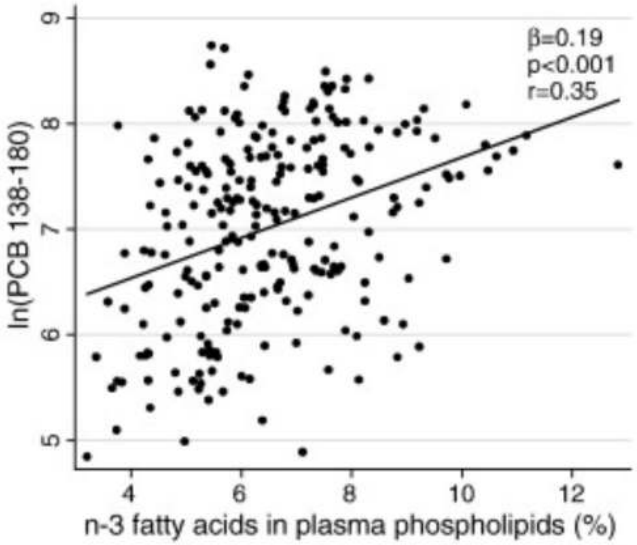
- These are **non-persistent** toxins.
- **Avoidance** is the primary strategy.
  - Must avoid **all** bisphenols.
- **Antioxidants** help protect from damage.

The five worst toxins:

Polychlorinated biphenyls (PCBs)

PCBs: correlation with fish consumption

Linear regressions between the proportion of very long-chain n – 3 fatty acids in plasma phospholipids and serum PCB concentrations.

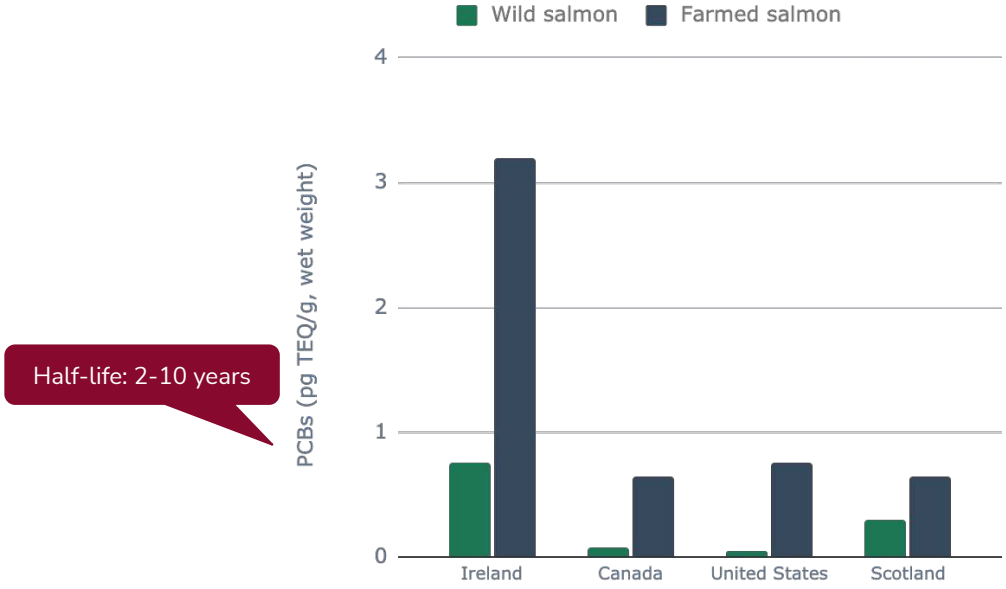


- Fish, especially farmed, is a significant source of PCBs.

[Bjermo, H., et al. (2013). Fish intake and breastfeeding time are associated with serum concentrations of organochlorines in a Swedish population.]

PCBs: concentration in salmon

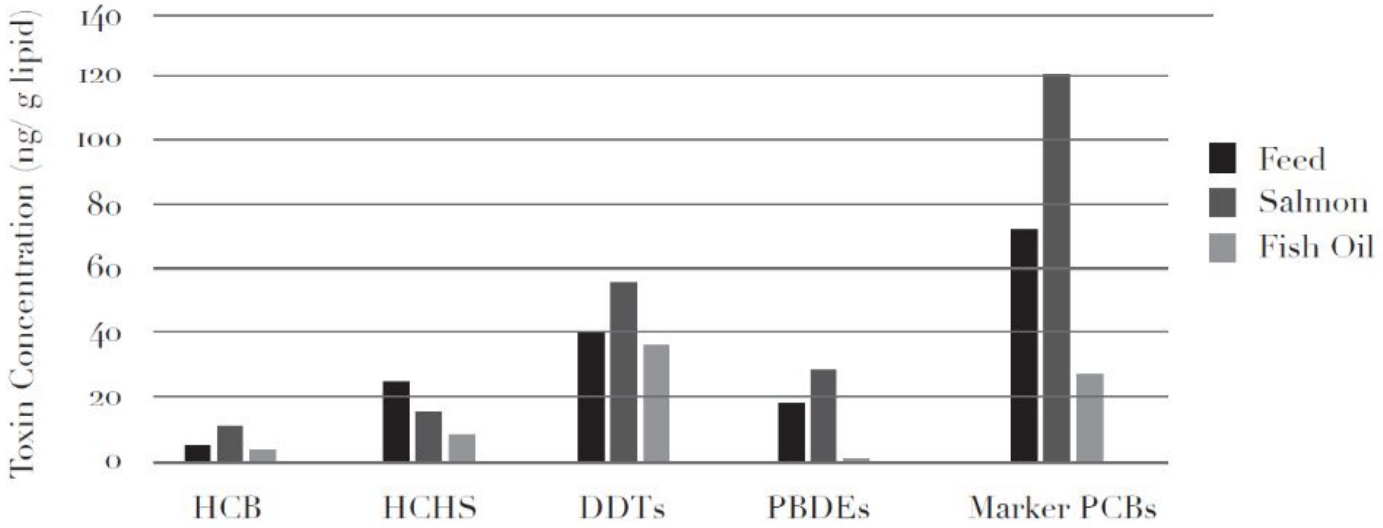
A growing number of studies show that farmed salmon contains more PCBs than wild salmon.



[Environmental Working Group. (n.d.). PCBs in farmed salmon.]

PCBs in farmed fish due to feed

Concentration of POPs in farmed Atlantic salmon, feed, and fish oil.



Jacobs, M. N., et al. (2002). Investigation of selected persistent organic pollutants in farmed Atlantic salmon (Salmo salar), salmon aquaculture feed, and fish oil components of the feed.

PCBs: % of disease due to PCBs

Disease	Threshold	% above threshold	Odds ratio	% of disease
Infertility, female	Fish eating	Baltic vs. Atlantic	2.5	↓46% fertility
Infertility, male	Pregnant vs. non-pregnant	N/A	N/A	↓22-38% fertility
Diabetes	104 ng/g (PCB 153)	25%	2.4	26%
Myocardial infarction	286 ng/day	25%	2.2	23%

Axmon, A., et al. (2000). Time to pregnancy and infertility among women with a high intake of fish contaminated with persistent organochlorine compounds.

Bergkvist, C., et al. (2015). Dietary exposure to polychlorinated biphenyls and risk of myocardial infarction - a population-based prospective cohort study.

Buck Louis, G. M., et al. (2013). Persistent environmental pollutants and couple fecundity: the LIFE study.

Song, Y., et al. (2016). Endocrine-disrupting chemicals, risk of type 2 diabetes, and diabetes-related metabolic traits: A systematic review and meta-analysis.

PCBs: % of disease due to PCBs

Disease	Threshold	% above threshold	Odds ratio	% of disease
Rheumatoid arthritis	Quartiles	25%	2.2-2.9	18-28%
ADHD	1.04 ng/g	25%	1.8	16%
Breast cancer (PCB 138)	39.6 ng/g creatinine	20%	3.2	63%
Breast cancer (PCB 138)	1.08 ng/g lipid	60%	1.9	36%

Lee, D.-H., et al. (2007). Positive associations of serum concentration of polychlorinated biphenyls or organochlorine pesticides with self-reported arthritis, especially rheumatoid type, in women.

Morgan, M., et al. (2017). Environmental estrogen-like endocrine disrupting chemicals and breast cancer.

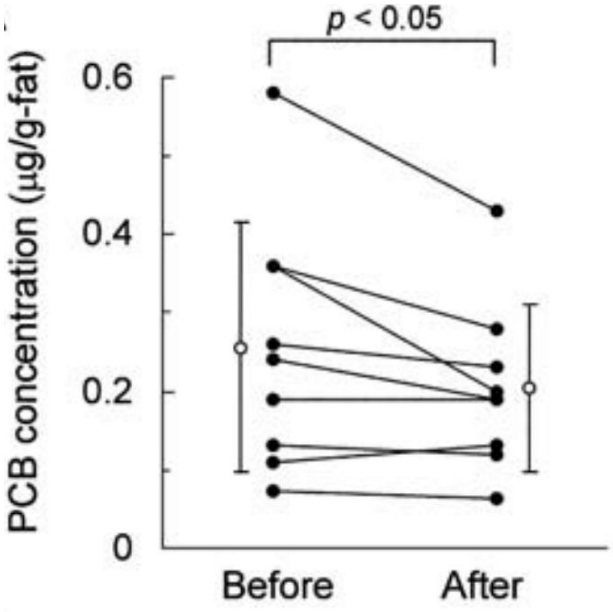
Recio-Vega, R. (2011). Serum levels of polychlorinated biphenyls in Mexican women and breast cancer risk.

Sagiv, S. K. (2010). Prenatal organochlorine exposure and behaviors associated with attention deficit hyperactivity disorder in school-aged children.

Colestimide reduces PCBs

Blood level of PCBs before and after colestimide treatment in nine subjects.

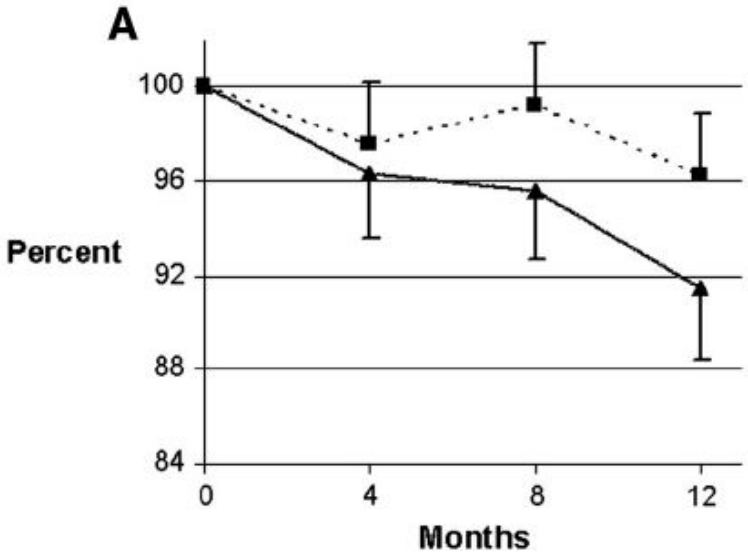
- Dose: 5 g/d
- Duration: 6 months
- Average reduction: 23%
- Those who did not take increased by 24%.



Sakurai, K., et al. Colestimide reduces blood polychlorinated biphenyl (PCB) levels..

Olestra reduces PCBs and DDE

Percent of change from baseline for total PCBs.



- Participants consumed potato chips made with olestra or vegetable oil.
  - 12-month duration
  - 15 g of olestra per day
  - 22 Pringles Light crisps
- No change in diet.
- Higher body fat = lower % decrease.
- 25% of participants experienced loose stools.
- Half-life was decreased from 20+ years to 8.5 years.

Jandacek, R. J., et al. (2014). Reduction of the body burden of PCBs and DDE by dietary intervention in a randomized trial.

PCBs: assessment

- Blood testing is best.
  - Typically adjusted to lipid levels and reported as ng/g lipid.
  - The lower, the better!
  - Mainly use to testing to monitor efficacy.

PCBs: intervention

Supplementation

- Fiber: try for total of 50 g/d

Diet

- Choose wild fish; avoid farmed fish.

Lifestyle

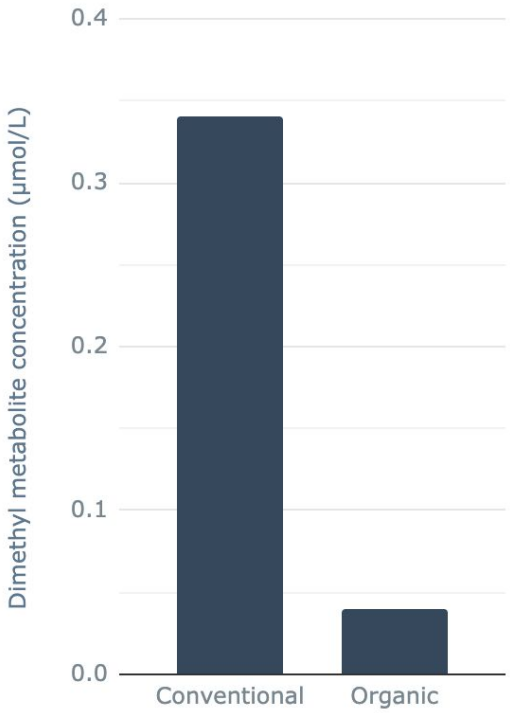
- Sauna regularly; at least once per week.

If levels are high and not decreasing with intervention, add **bile sequestrants**.

General intervention

Pesticide load in food

- Study in Seattle of children eating 75% organically-grown versus 75% chemically-grown foods
- **10-fold increase** in pesticides doubles ADHD

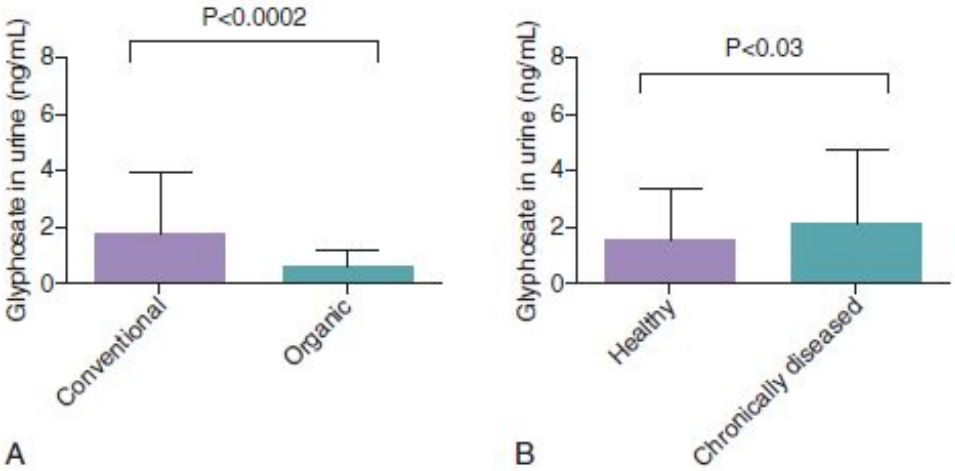


Bouchard, M. F., et al. (2010). Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides.

Curl, C. L., et al. (2003). Organophosphorus pesticide exposure of urban and suburban preschool children with organic and conventional diets.

Eat organic food

Eating organic food decreases glyphosate levels, and chronically ill people have higher glyphosate levels.

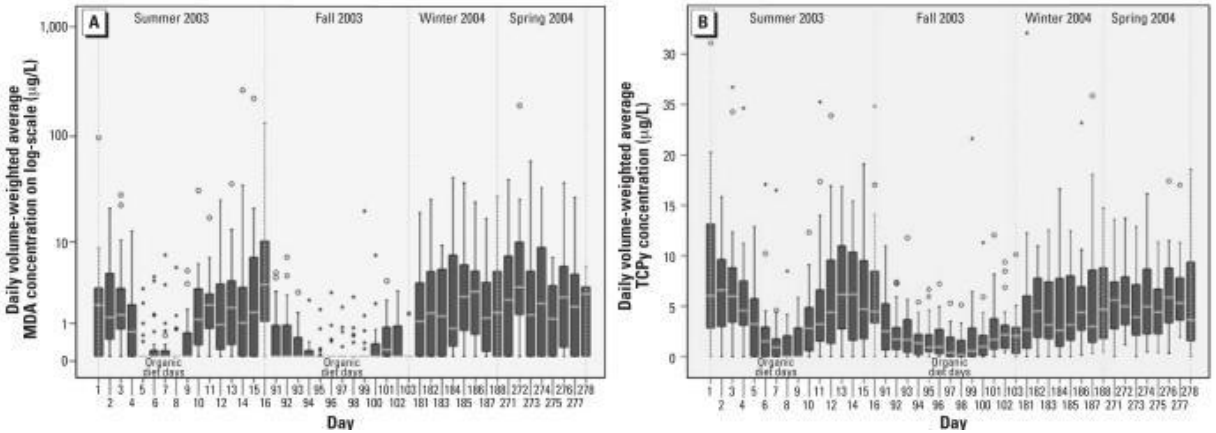


- Healthy people have lower glyphosate levels.
- Glyphosate levels are a measure of Roundup exposure.

Goen, T., et al. (2017). Efficiency control of dietary pesticide intake reduction by human biomonitoring.

Eat organic food

It only takes a few days of eating organically to greatly decrease toxic load.



- Twenty-three children three to 11 years of age.
- Pesticide levels drop dramatically within three days.

[Lu, C., et al. (2008). Dietary intake and its contribution to longitudinal organophosphorus pesticide exposure in urban/suburban children.]

Wash conventional food

Washing chemically-grown foods has been found to decrease pesticides.

Generally, acid washes are most effective.

TABLE 3.12 Reduction of Chlorinated Pesticide Residue with Water, Acid, and Alkaline Washes, %

Solution	Lindane	Aldrin	Heptachlor Epoxide	o,p-DDE	p,p-DDE	o,p-DDD
Radish–5 conc.	100	100	100	67.6	100	100
Radish–10 conc.	100	100	100	73.1	100	100
Acetic acid–5 conc.	66.7	72	95.2	75.2	96.1	96
Acetic acid–10	78.3	84	96.6	86.7	97.4	97.4
Citric acid–5	100	76	100	73.1	98	100
Citric acid–10	100	85.2	100	77.5	18.4	100
Ascorbic acid–5	100	84	100	57.5	91.9	100
Ascorbic acid–10	100	90.8	100	67.6	94.9	100
H_2O_2–5	81.2	64	94.5	80.4	100	100
H_2O_2–10	89.1	78	95.9	87	100	100
Tap water	12	10	9.8	2	3.5	3.9
Na_2CO_3–5	89.1	84	93.2	NA	NA	NA
Na_2CO_3–10	92	88	95.2	NA	NA	NA

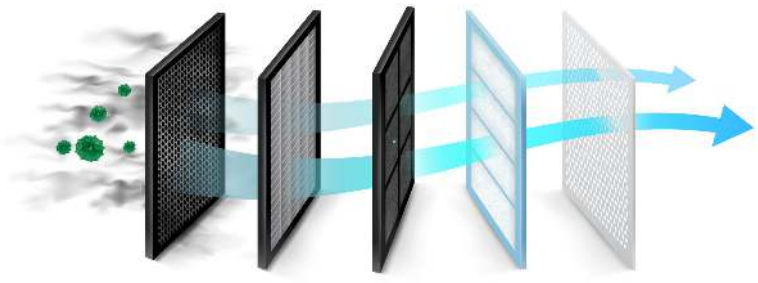
Modified from Zohair, A. (2001). Behavior of some organophosphorus and organochlorine pesticides in potatoes during soaking in different solutions. *Food and Chemical Toxicology*, *39*(7), 751-755.

Zohair, A. (2001). Behaviour of some organophosphorus and organochlorine pesticides in potatoes during soaking in different solutions.

Filter the air

Eating organic food decreases glyphosate levels, and chronically ill people have higher glyphosate levels.

- Whole-house air filter
  - Merv-8 (at least), running 24/7.
  - Otherwise, use HEPA filters in main rooms.
- Take off shoes before entering the house.
- Declare the house a scent-free zone.
- Filter outdoor air for fresh circulation.
- Use toxin-absorbing plants to help decrease chemicals in the air.



Goen, T., et al. (2017). Efficiency control of dietary pesticide intake reduction by human biomonitoring.

Filter the air

As little as two days in a clean room can improve health.

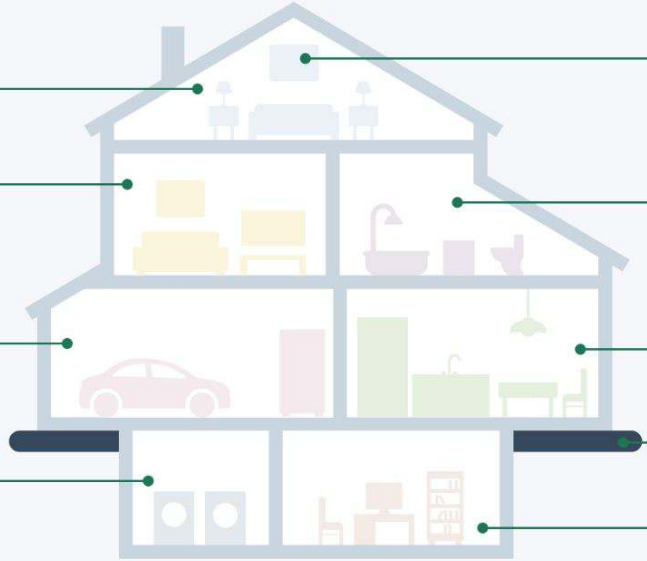
Marker	Change
Systolic blood pressure	↓ Avg. 2.7 mm
Diastolic blood pressure	↓ Avg. 4.8 mm
Exhaled nitrous oxide	↓ 17%
IL-1B	↓ 58%
Myeloperoxidase	↓ 33%
Monocyte chemoattractant protein	↓ 1-17.5%

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

Chen, R., et al. (2015). Cardiopulmonary benefits of reducing indoor particles of outdoor origin: A randomized, double-blind crossover trial of air purifiers.

Improving air quality in your home

Fullscript



Bedroom

Install a carbon monoxide (CO) alarm close to bedrooms.

Living room

Reduce the use of incense and candles.

Vacuum carpets with a high-efficiency particulate air (HEPA) filter.

Do not smoke inside.

Garage

Avoid idling gas-powered machinery inside your garage.

Ensure the door between your home and attached garage is sealed properly.

Laundry room

Ensure your dryer efficiently vents air towards the outside and isn't blocked.

Windows

Open windows and doors to let fresh air inside.

Open windows and doors when exposed to VOCs (e.g., when painting)

Bathroom

Use the exhaust fan during and after you shower.

Repair damaged grout, caulking, or tiles to avoid mold growth.

Clean up and remove mold with soap and water.

Kitchen

Never use a fuel-burning grill inside (e.g., BBQ).

Below the house

Measure the radon levels in your home.

Basement

Make sure gas-fueled appliances (e.g., furnace) are well-maintained.

Plants that absorb air chemicals

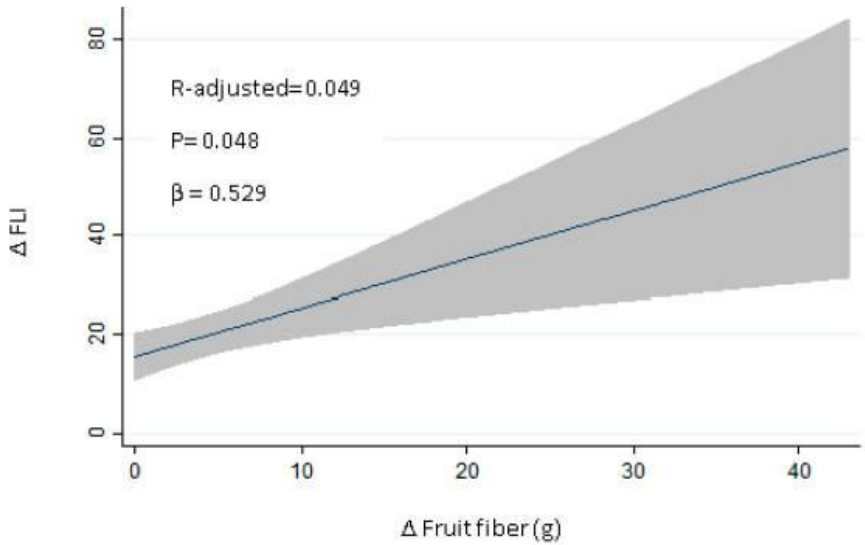
Percentage of chemicals removed from a sealed chamber by houseplants in a 24-hour period NASA study.

Plant	Formaldehyde	Benzene	Trichloroethylene
Mass cane	70	21.4	12.5
Pot mum	61	53	41.2
Gerber daisy	50	67.7	35
Wernicke	50	52	10
Ficus	47.4	30	10.5
Leak control	2.8	5	10

Wolverton, B. C., et al. (1989). Interior landscape plants for indoor air pollution abatement.

Fiber for liver detoxification

Fiber blocks enterohepatic recirculation.



Improvement in:

- Fatty liver index (FLI)
- Hepatic steatosis index (HIS)
- Nonalcoholic fatty liver disease (NAFLD) liver fat score
- Gamma-glutamyl transferase (GGT)

Benefits begin at **8.8 g fruit fiber/d.**

Note: the graph is amount of decrease in FLI.

Cantero I, et al. (2017). Fruit fiber consumption specifically improves liver health status in obese subjects under energy restriction.

Increase glutathione levels

Glutathione is essential to protecting the liver from free radicals produced during detoxification.

Supplementation

- Topical or liposomal glutathione
- NAC: 500 mg once or twice a day
  - Or whey powder: 15 g/d
- Resveratrol: 1 g/d

Diet

- Almonds, 83 g/d
- Non-alcoholic beer: 1 pint a day

Lifestyle

- Exercise: both aerobic and strength training
- Meditation: daily

Foundational strategies

Avoidance is key.

- The half-life of PCBs is 3 to 25 years.
- Choose wild fish; avoid farmed fish.

Include **fiber**.

- Rice bran: 10 g/d

Sauna regularly.

- Sweating is key, the type of sauna is mainly for convenience.
- At least 20 minutes of heavy sweating, 1-4 times a week.

If PCBS, use **bile sequestrants**.

- This includes holestimide, cholestyramine, and olestra.

Foundational strategies

Practice patience; don't expect the speed of results seen with a drug or even nutrition therapy.

Identify and stop the **exposure**.

Greatly decrease the **body's load**.

- Some toxins become apparent only after others are removed.

For **damaged enzymes** to work:

- Must displace the enzyme poison with nutrient cofactor, or
- Degrade and replace the enzyme.
  - Half-life of MAO-B in baboon brain = 30 days.

Finally, the damage has to be **repaired**.

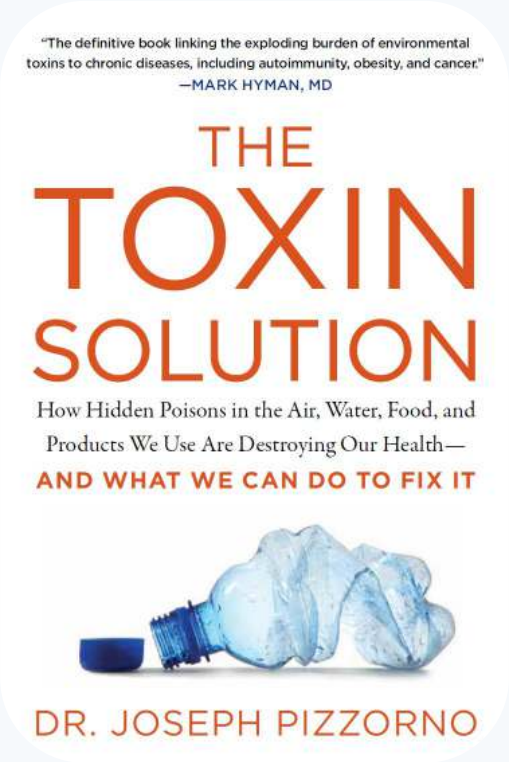
Arnett, C. J., et al. (1987). Turnover of brain monoamine oxidase measured in vivo by positron emission tomography using L-[11C]deprenyl.

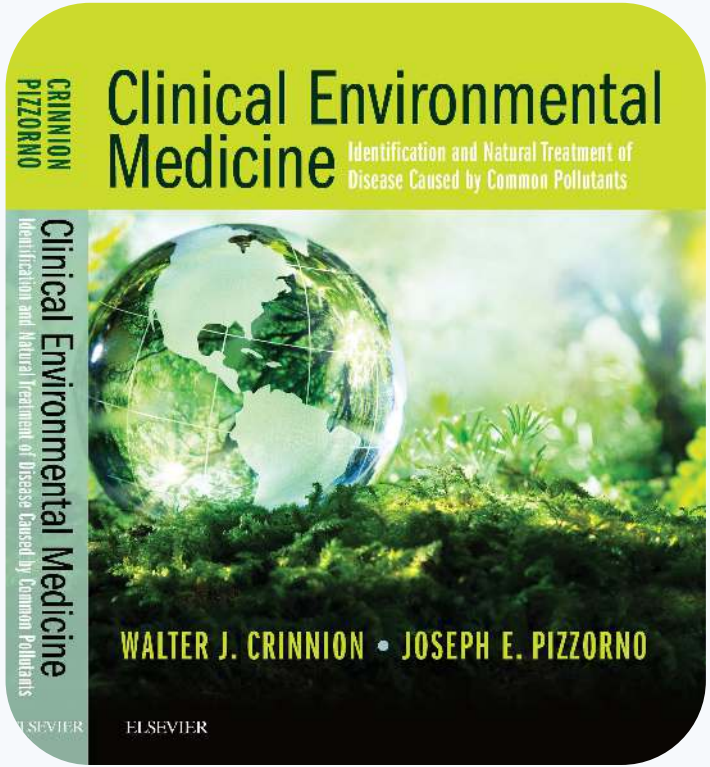
Summary

Summary

- Toxins are **ubiquitous** in the industrialized world.
- Toxins have become the **primary drivers of chronic disease**.
- **Five toxins** account for most of the damage.
- **Avoidance** is critical.
- Toxin **elimination** can be facilitated with diet, nutrition and saunas.

Further reading





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