

Perfluorinated Alkyl Substances (PFAS)

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Boston Children's Hospital
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I do not intend to discuss an unapproved/investigative use of a commercial drug/product/device in my presentation.





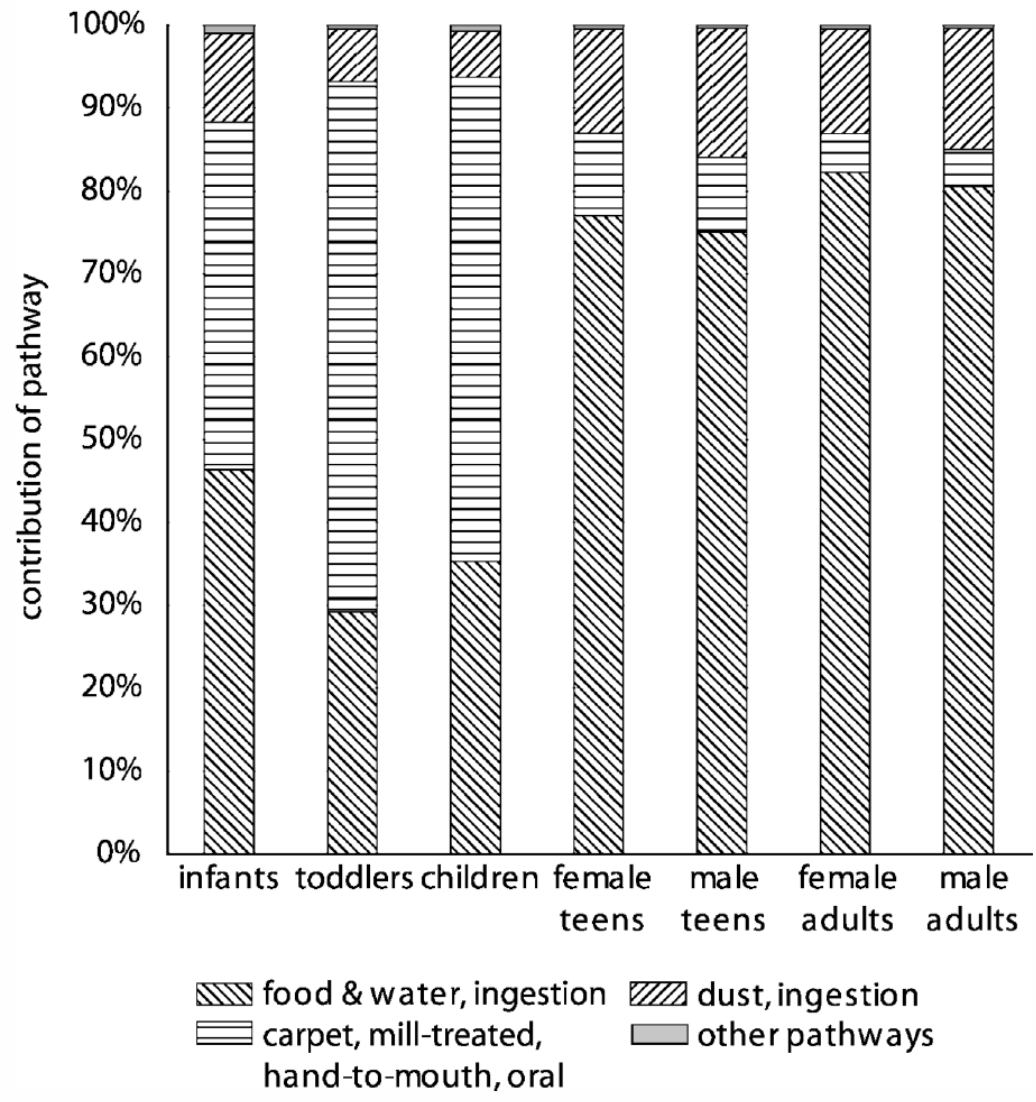
Definition, Chemistry, Uptake
Water studies
Animal studies
C8 health study
Human studies
Clinical perspectives
Recommendations

Properties of PFAS

- Water & Oil Repellant
- >350 different congeners
- Thousands of tons per year
- PFOA - perfluorooctanoate
- PFOS – perfluorooctane sulfonate
- PFHx – perfluorohexanoate
- PTFE - polytetrafluoroethylene
- Non-volatile
- Half life 4-8 years, persistent
- 3M Company d/c PFOS production in 2002
- International (2006) agreed d/c PFOA by 2015



Pathways of PFOS Exposure



PFOS above the EPA PHA

- The EPA and DES asked the Air Force to test the wells on the Tradeport for PFCs in April 2014
- 3 wells that supply drinking water: Haven, Harrison, & Smith Wells
- Water blended at the treatment plant prior to tap
- 594 Fire/Crash/Training DoD sites in U.S.

Wells	PFOS µg/L (April)	PFOA µg/L (April)
Haven	2.5	0.35
Harrison	0.048	0.009
Smith	0.018	0.0035

❖ PFOS PHA: 0.2 µg/L

❖ PFOA PHA: 0.4 µg/L



Site	PFOS (EPA 0.4 ppb or ug/L)	PFOA (EPA 0.2 ppb or ug/L)
PEASE, NH	2.5	0.35
Cologne, GR	8.35	0.16
Ohio & West Virginia "C8"	0.05	3.55
Ronneby, Sweden	4.0	0.13
Decatur, Alabama	0.114	0.394
Cottage Grove, MN	120	105
Yangtze River, China	0.014	0.26
River Po, Italy	0.01	1.3
Arctic Cap	pg/L	pg/L

Rumsby et al. Phil Trans R Soc A 2009; 367

PFAS: Animal Studies



- Altered gene expression and testosterone synthesis (Shi 2007)
- Behavioral (Ciu 2009; (Onischenko 2010)
- Reproductive (Fuentes 2006)
- Tumors (ATSDR 2009)
- Neonatal mortality (Luebker 2005)
- Increased liver weight (ATSDR, 2009; Ciu 2009)
- Reduced immunological function (Dewitt 2012)
- Adverse effects on mammary gland development (mice)(Post, 2012)

C8 (PFOA) Health Project, 2005-2006

- Environmentally exposed study of 69,030 participants from West Virginia and Ohio (Ohio-River Valley) exposed to PFOA from a Chemical Plant
- Link report: based on class action lawsuit settlement
- “Probable link” – (judicial opinion – not necessarily scientific) “more likely than not that among class members a connection exists between PFOA exposure and a particular human disease.”
- Those doing the studies rendered the opinion
- No studies of subsequent effects on community level of stress, health impacts, beliefs, or services utilization

http://www.c8sciencepanel.org/prob_link.html

Link Reports, 2011-2012

No “Probable Link” N=41

- HTN
- Coronary Heart Disease
- Stroke
- Chronic kidney disease
- Liver disease
- Osteoarthritis
- Parkinson’s disease
- Other autoimmune diseases (not UC)
- “Common infections” (i.e. influenza)
- Neurodevelopmental disorders, including ADHD and learning disabilities
- Asthma or COPD
- DM type 2
- Birth defects, miscarriage or stillbirths
- Preterm birth or low birth weight

“Probable Link” N=6

- High cholesterol
- Thyroid disease
- Ulcerative colitis
- Testicular cancer
- Kidney cancer
- Pregnancy-induced hypertension

http://www.c8sciencepanel.org/prob_link.html

“Endocrine Disruption”

- General term meaning there is question about PFCs affecting the endocrine system
- Exact mechanism for possible endocrine-related effects not fully understood
- Question whether developing infants are more susceptible

PFAS & Thyroid Function

Study	Sample	Site	Measure	Result
Knox - 2011	N=52,296 Xsection study	C8 Ohio Valley	T4, T3 Uptake, TSH, Albumen	No thyroid disease; gender differences; clinical insignif reduced T3 uptake, higher T4
Chan – 2011	N=96 HypoT4 pregnant women; N=175 controls	Edmonton, Alberta, Canada	PFOS, PFOS, PFHxS	No association with hypoT4emia

Study	Sample	Site	Measure	Result
Bellinger – 2013	N=320 Ages 6-12 yr	C8 Ohio Valley	IQ, Read, Math, Lang, Attention	+++ <i>in utero</i> PFOA scored higher IQ
Fei – 2008	N=1400 pairs Pregnancy PFOA, PFOS+ infants (6 & 18 months)	Denmark	Developmental milestones	No association
Liew – 2015	220 ADHD, 220 Autism, 550 matched controls	Denmark	PFOS, PFOA	No assoc: ADHD, Autism
Hoyer – 2014	Pregnancy (N=1106), 5-9 year olds	Ukraine, Poland	Motor development, activity	Possibly hyperactive?

Original Article

Perfluorocarbon exposure, gender and thyroid function in the C8 Health Project

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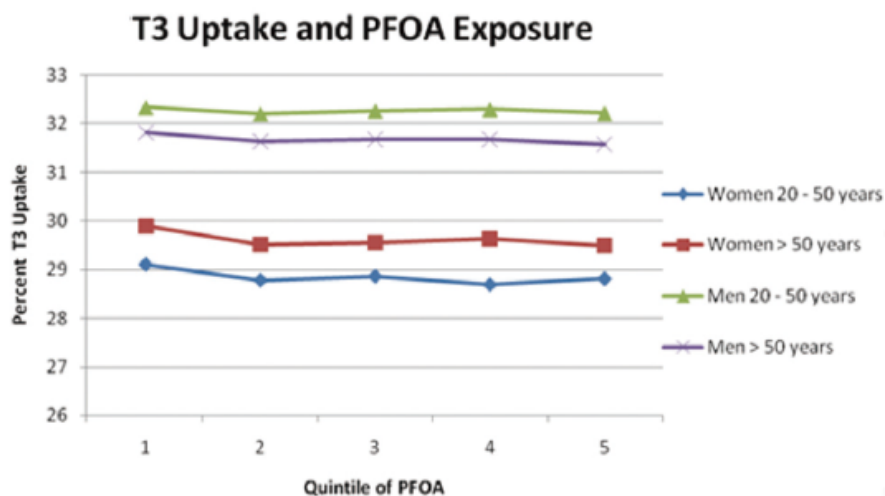


Fig. 2. Serum T₃ Uptake by PFOA Quintile*. * Quintiles in ng/ml. Quintile 1 = 0.25 – 11.8, Quintile 2 = 11.9 – 17.0, Quintile 3 = 17.1 – 22.4. Quintile 4 = 22.5 – 30.7, Quintile 5 = 30.8 – 564.3.

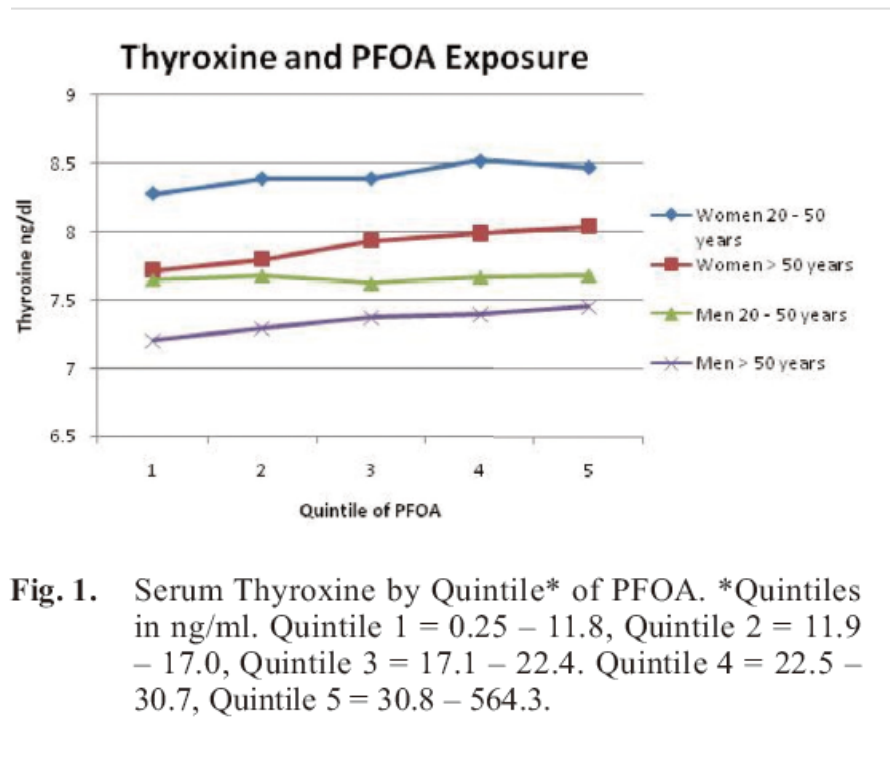


Fig. 1. Serum Thyroxine by Quintile* of PFOA. *Quintiles in ng/ml. Quintile 1 = 0.25 – 11.8, Quintile 2 = 11.9 – 17.0, Quintile 3 = 17.1 – 22.4. Quintile 4 = 22.5 – 30.7, Quintile 5 = 30.8 – 564.3.

Albumin and PFOA Exposure

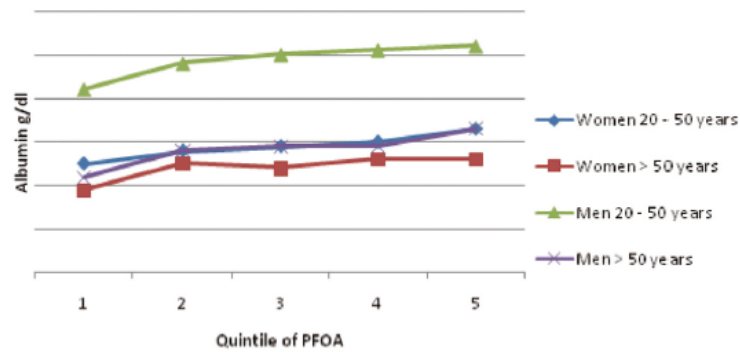


Fig. 3. Serum Albumin by PFOA Quintile*. *Quintiles in ng/ml. Quintile 1 = 0.25 – 11.8, Quintile 2 = 11.9 – 17.0, Quintile 3 = 17.1 – 22.4, Quintile 4 = 22.5 – 30.7, Quintile 5 = 30.8 – 564.3.

Thyroxine and PFOS Exposure

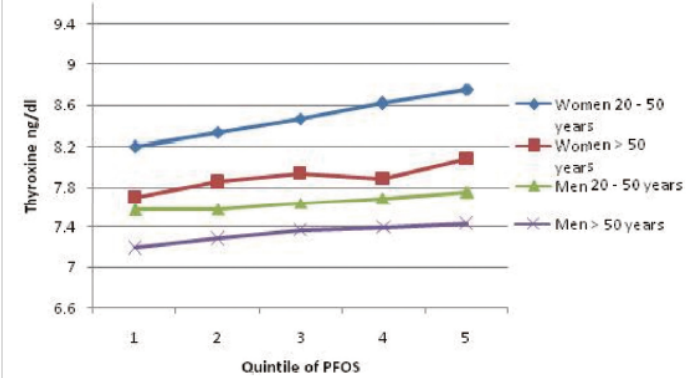


Fig. 4. Serum Thyroxine by PFOS Quintile*. *Quintiles in ng/ml. Quintile 1 = 0.25 – 11.8, Quintile 2 = 11.9 – 17.0, Quintile 3 = 17.1 – 22.4, Quintile 4 = 22.5 – 30.7, Quintile 5 = 30.8 – 564.3.

T3 Uptake and PFOS Exposure

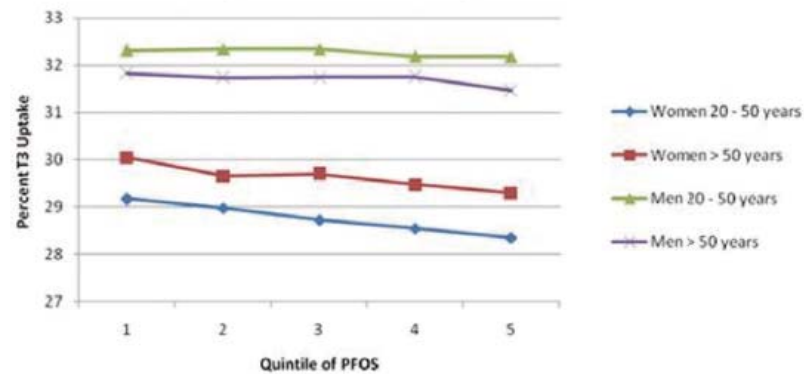


Fig. 5. Serum T₃ Uptake by PFOS Quintile*. * Quintiles in ng/ml. Quintile 1 = 0.25 – 11.8, Quintile 2 = 11.9 – 17.0, Quintile 3 = 17.1 – 22.4, Quintile 4 = 22.5 – 30.7, Quintile 5 = 30.8 – 564.3.

Study	Sample	Site	Measure	Result
Eriksen – 2009	N=57,053 pros cohort; 1240 tumors vs 772 controls	Denmark	Prostate, bladder, liver, pancreas CA	No Association with 4 cancers
Chang – 2014	Meta-Analysis of 18 PFOA,PFOS epi studies	Worldwide	Kidney, Liver, Testicular, Leukemia, Lymphoma, colorectal cancer	Misclassify bias, No Association found or inverse relationship (colorectal)
Barry – 2013	N=32,254 adults + workers, PFOA only; N=2507 cancers	DuPont Plant workers + Ohio Valley residents	21 cancer types	Association only with Testicular Cancer

Study	Sample	Site	Measure	Result
C8 Health Study Panel – 2011	N=12,000 pregnancies 1990-2005	C8 Ohio Valley	LBW, Miscarriage, Birth Defects	No association

Study	Sample	Site	Measure	Result
Grandjean 2012	N=587 5&7 year olds	Faroe Islands	PFOA, PFOS, DT Ab	Danish vaccine?PCBs ? MeHg? Lowered Abs: 18 7 yr olds with lower T 32 with lower P Not same kids



Endocrine Effects Studied

- Studied health effects related to endocrine system:
 - Low birth weight
 - Child growth and development
 - Delay in puberty and sexual development
 - Thyroid hormone
 - Obesity/Lipid metabolism
- Studies have shown inconsistent findings
- We cannot be sure about what health effects might occur as a result of PFC exposure

What do these studies tell us clinically?

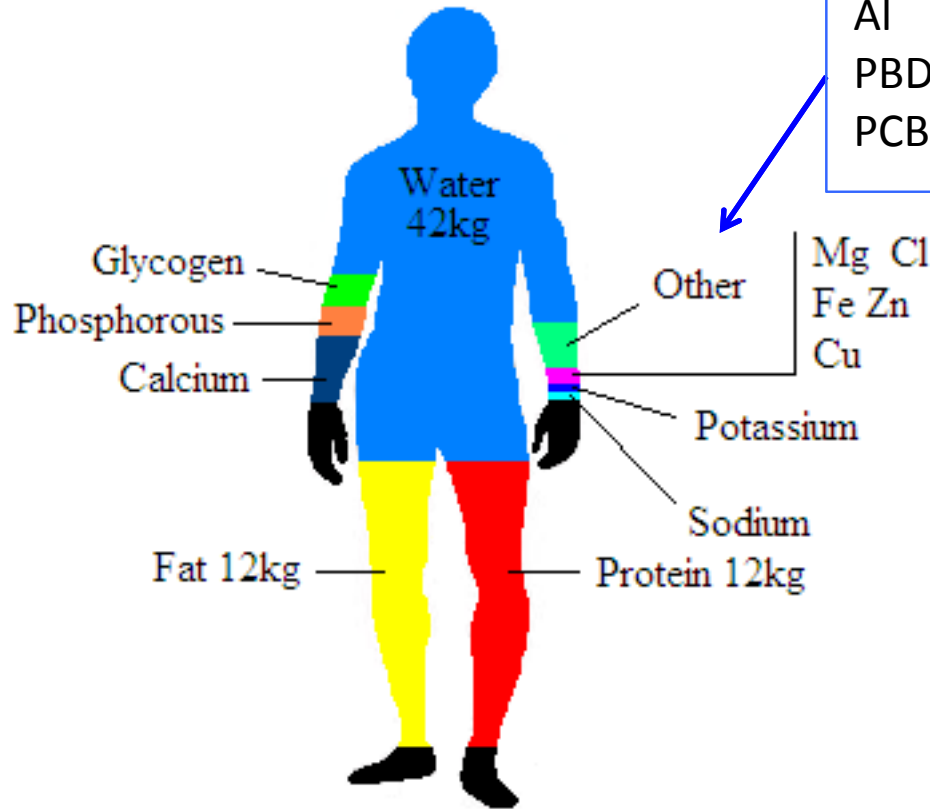
- Many epi studies are observational: cannot assign cause
- Statistical Significance does not = Clinical Significance
- Every study has flaws; needs to be plausible/replicated
- Publication Bias

- LC-electrospray ionization MS sensitive to pg/m³ or pg/L
- Just because a chemical can be detected in a body tissue or fluid does not mean it is causing a health effect
- Just because it can be removed from the body doesn't necessarily make you healthier

- We try to practice evidence-based medicine, medicine based on ALL the evidence (we don't always succeed!)

1mg/L = 1 ppm
1 ug/L = 1 ppb
1 ng/L = 1 ppt
1pg/L = 1 ppq

Pb 10-20 ug/L
PFAS 3-4 ug/L
Al 15 ug/L
PBDE 28 ng/gm lipids
PCB 0.5-2.0 ug/L



National Health & Nutrition Examination Study (NHANES)

2003-2004

Ages: >12 years

N=2,094

Units in ug/L

Max PFOS 435 ug/L

Max PFOA 77.2 ug/L

	Mean	10 th %tile	25 th %tile	90 th %tile	95 th %tile
PFOS	20.7	9.8	14.6	41.2	54.6
PFOA	3.9	1.9	2.7	7.8	9.8

Cottage Grove, MN 3M worker: 114,100 ug/L

Tangxun Lake, Wuban, Chinese fisherman – 31,400 ug/L

Arctic polar bear liver: 1.7-4.0 ug/gm

Source: Calafat AM et al. Environ Heal Persp 2007; 115 (11): 1596-1602



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Summary for the First 98 Participants

- Compared to other communities exposed to environmental contamination and with chemical plant workers:
 - Average PFOA, PFOS, and PFHxS blood levels from adults at the Tradeport are **lower...**

First 98 results vs U.S. Population

PFC Tested	Geometric Mean, first 98 samples (µg/L)	Levels in the U.S. Population (µg/L)*		
		Range	Geometric Mean	95 th Percentile
PFOA perfluorooctanoic acid	3.20	0.07-43	2.08	5.68
PFOS perfluorooctane sulfonic acid	8.08	0.14-235	6.31	21.7
PFHxS perfluorohexyl sulfonate	4.79	0.07-47.8	1.28	5.44
PFUA perfluoroundecanoic acid	0.20	0.07-6.96	**	0.620
PFOSA perfluorooctane sulfonamide	0.10	0.07-0.62	**	<LOD
PFNA perfluorononanoic acid	0.69	0.06-80.77	0.881	2.54
PFDeA perfluorodecanoic acid	0.21	0.07-17.8	0.199	0.690
Me-PFOSA-AcOH2 2-(N-methyl-perfluorooctane sulfonamido) acetic acid	0.15	0.06-4.25	**	0.690
Et-PFOSA-AcOH 2-(N-ethyl-perfluorooctane sulfonamido) acetic acid	0.14	0.07-0.72	**	0.110

(µg/L) = micrograms per liter

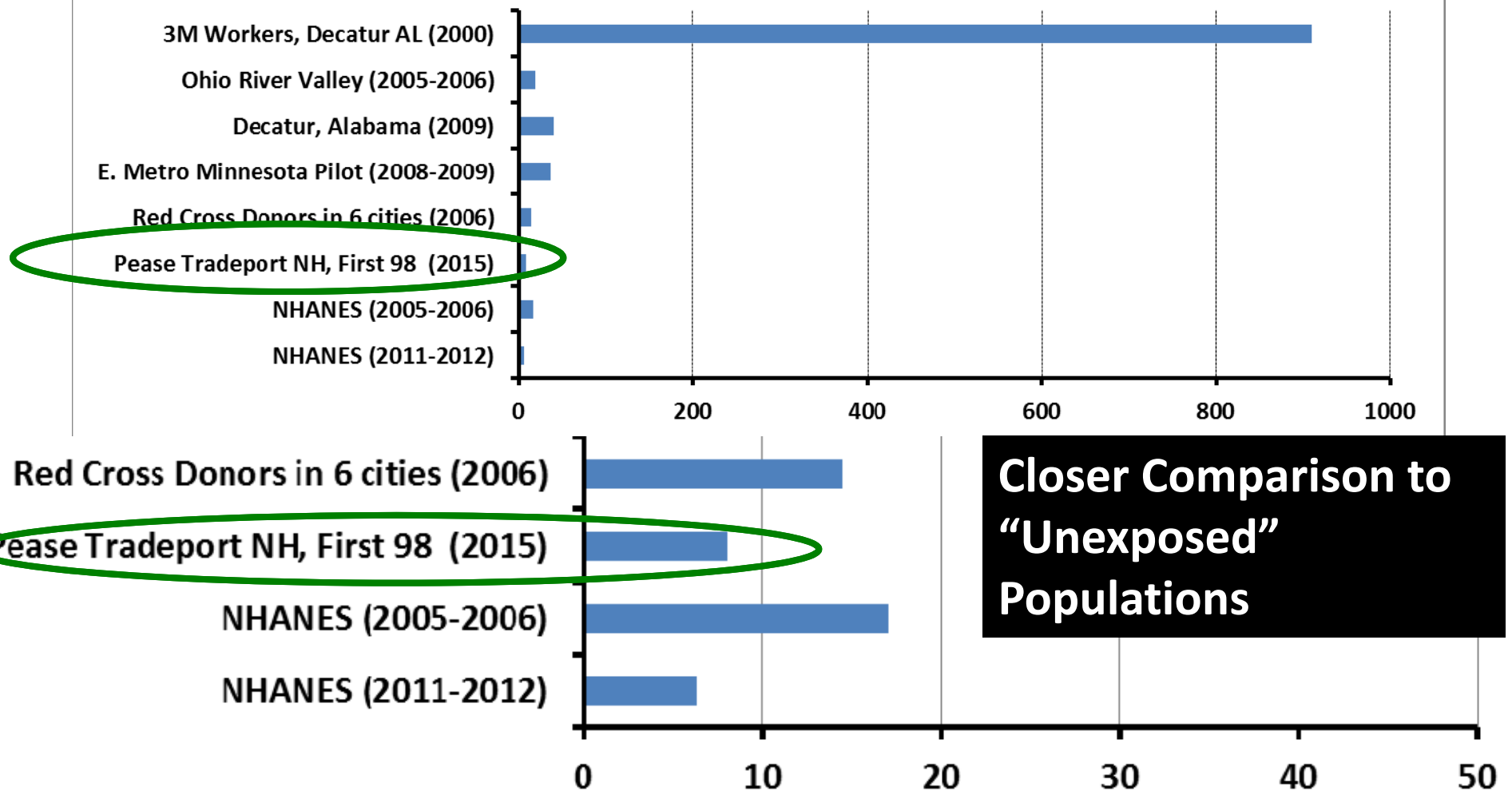
LOD = limit of detection (0.01 µg/L)

*Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables (February, 2015) for specimens collected 2011-2012.

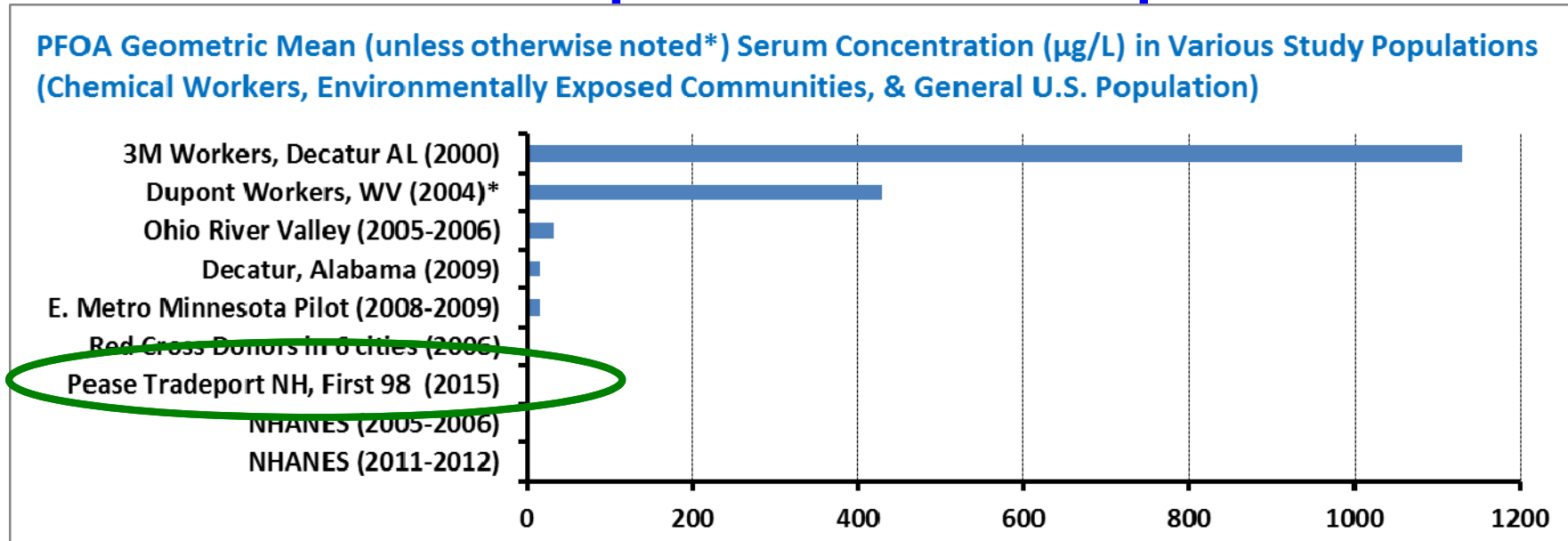
** The national average was not calculated for this PFC, as the proportion of results below limit of detection was too great to provide a valid result.

PFOS Comparisons: Other Populations

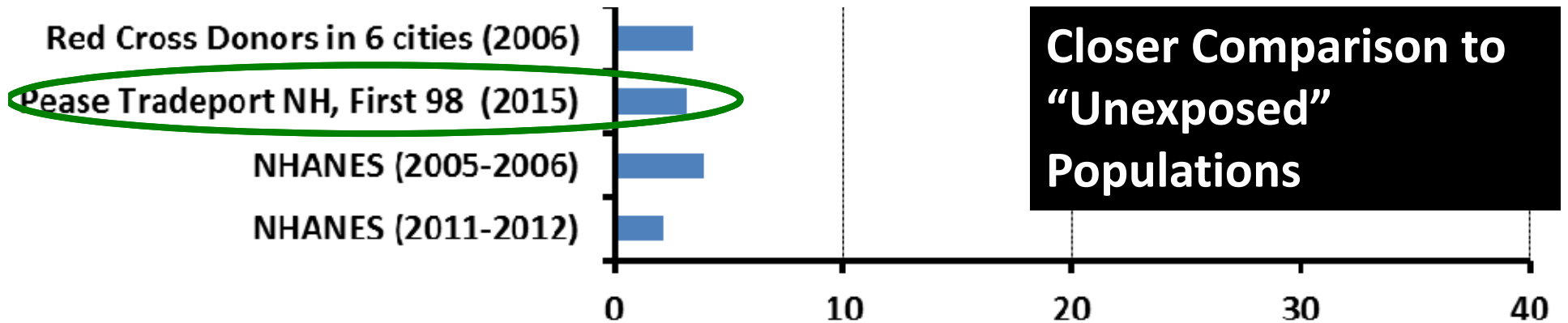
PFOS Geometric Mean Serum Concentration ($\mu\text{g/L}$) in Various Study Populations
(Chemical Workers, Environmentally Exposed Communities, & General U.S. Population)



PFOA Comparisons: Populations

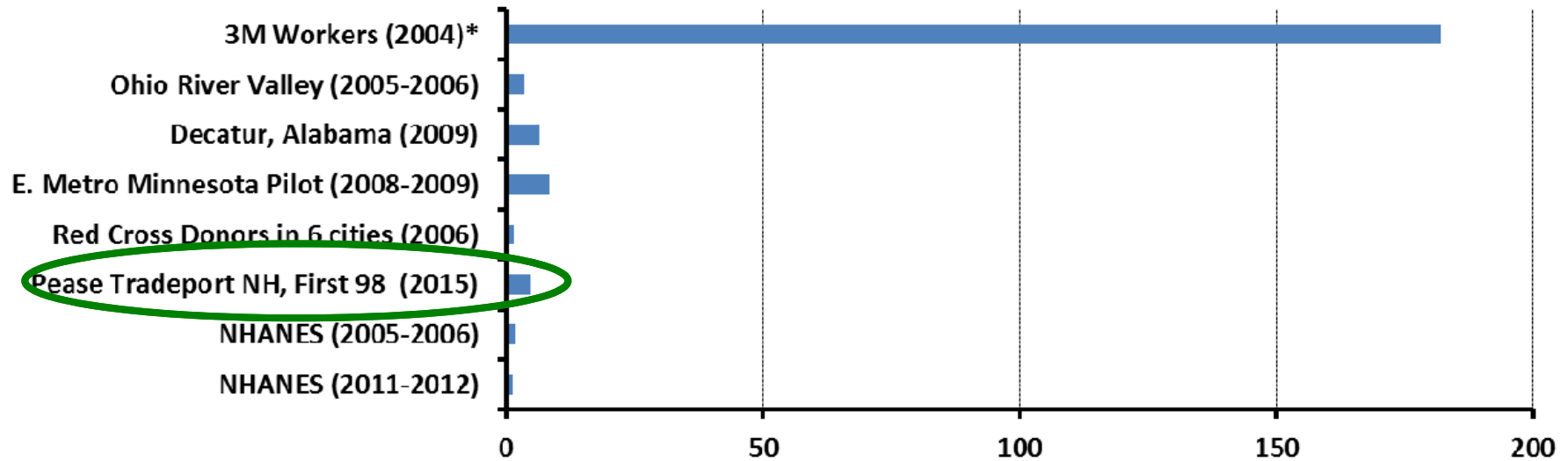


* Indicates Arithmetic mean reported (usually higher than geometric mean).



PFHxS Comparisons: Populations

PFHxS Geometric Mean (unless otherwise noted*) Serum Concentration ($\mu\text{g/L}$) in Various Study Populations (Chemical Workers, Environmentally Exposed Communities, & General U.S. Population)



**Closer Comparison to
“Unexposed” &
Environmentally
Exposed Populations**

Government Agencies Speak

- NH (June 2015) “...the levels found in blood do not predict what, if any, health impact may occur.”
- ATSDR (June 2015) “test results cannot currently be used to predict health effects, nor can they be linked to specific health problems”
- ATSDR (June 2015) “test results cannot, in general, be used to specifically predict sources of exposure”



My Questions For You

- What will I do to reduce my family's exposure to PFAS?
- What will they replace PFAS with?
- How will I insure that my drinking water is safe?
- How will I know if any new health effects of PFAS are confirmed or new strategies recommended?

POU Treatment Devices

500 gallons

- **DES Drinking Water Groundwater Bureau**
 - (603) 271 2513
- **Test all private wells**
- **BRITA & PUR filters (may not work?)**
- **AC Devices**
 - Culligan RC-EZ-4
 - Kenmore Elite 625 385010
- **RO Devices**
 - Culligan Aqua Cleer
 - GE Smartwater (GXRM10GBL)



Recommendations to Healthcare Providers

- Perform routine diagnostic and screening tests as normal based on a thorough history, physical exam, and assessment
- No specific testing or screening is recommended based on PFC levels
- There is no way to connect specific health problems to PFC levels
- Repeat PFC testing is not medically indicated or recommended
- DHHS has recommendations for how to reduce PFC exposure

Healthcare Provider Resources

- NH DHHS (800) 852-3345
- NNE PCC (800) 222-1222
- DHHS Website for additional Information:
<http://www.dhhs.state.nh.us/dphs/investigation-pease.htm>
- Boston Environmental Health (requires a provider referral):
 - **Adult:** 617 665 1580
 - **Child:** 617 355 8177
- Questions about PFCs and Testing directed to DHHS: (603) 271 9461

Replacement for PFAS

- *Perfluorobutane Sulfonyl Fluoride (PFBS)*
 - *Made by 3M*

