Health Effects of Per- and Poly-Fluoroalkyl Substances and Occupational Relevance to Military Firefighters

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  - Department of Defense
  - Department of the Army
  - Department of the Navy
  - Department of the Air Force

- No financial or organizational interests

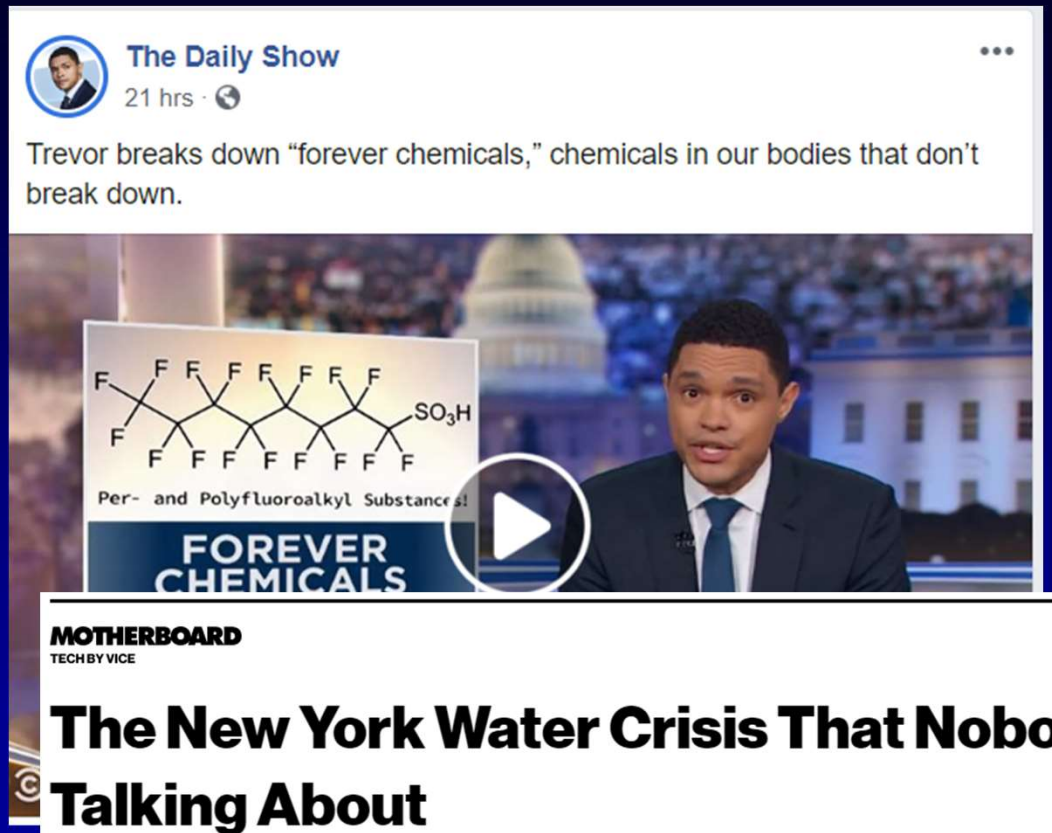
Learning Objectives

- Describe the commonly identified sources of PFAS in the environment
- Describe the currently known basic toxicology and health effects of PFAS
- Develop an approach for responding to firefighter inquiries re: health effects of PFAS

Theoretical Case

- Firefighter requests information
- Perfluorohexane sulfonic acid (PFHxS)

Why Are We Here?



TESTING *for* PEASE

Business

Major restaurant chains commit to eliminating ‘forever chemicals’

Several restaurant brands react after Consumer Reports finds dangerous chemicals linked to serious health problems widespread in fast food packaging

By Laura Reiley

March 24, 2022 at 3:03 p.m. EDT

MOTHERBOARD
TECH BY VICE

The New York Water Crisis That Nobody's Talking About

For years, "forever chemicals" flowed into Newburgh's drinking water.
It turns out they came from a nearby air base.

Why Are We Here?

Health.mil
The official website of the Military Health System

Contact U

About the MHS | Topics | Training | Policies | Reference Center | News & Gallery

MHS Home > Military Health Topics > Combat Support > Public Health > PFAS

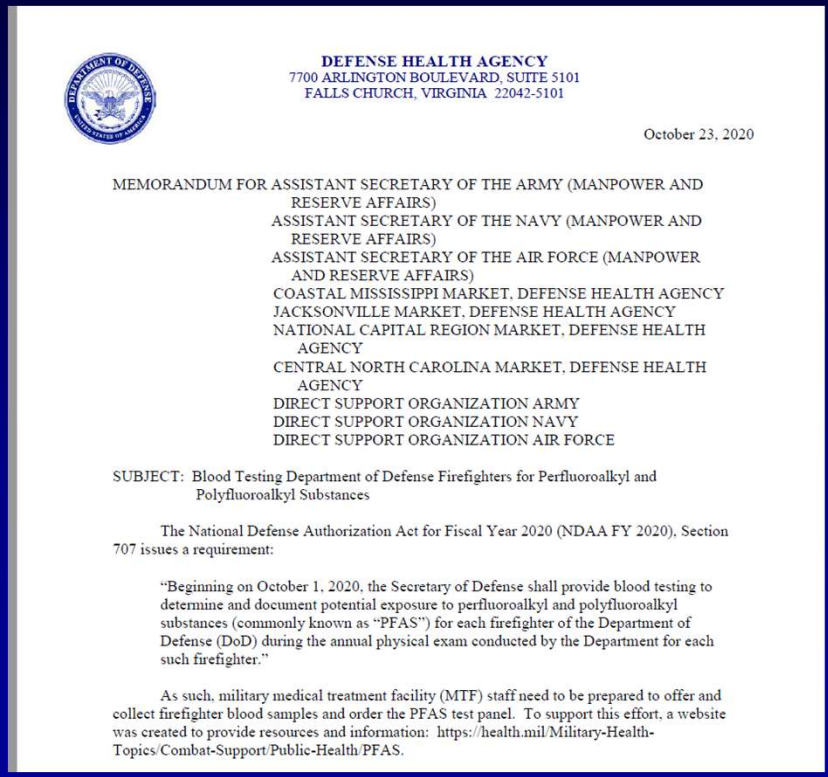
Combat Support

- Armed Forces Health Surveillance Division
- Armed Forces Medical Examiner System
- Armed Services Blood Program
- Defense Medical Readiness Training Institute

Perfluoroalkyl and Polyfluoroalkyl Substances

According to the CDC, perfluoroalkyl and polyfluoroalkyl substances (PFAS) are a large group of man-made chemicals that have been used in industry and consumer products worldwide since the 1950s.

- PFAS do not occur naturally, but are widespread in the environment.
- PFAS are found in people, wildlife and fish all over the world.
- Some PFAS can stay in people's bodies a long time.
- Some PFAS do not break down easily in the environment.



DEFENSE HEALTH AGENCY
7700 ARLINGTON BOULEVARD, SUITE 5101
FALLS CHURCH, VIRGINIA 22042-5101

October 23, 2020

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE NAVY (MANPOWER AND RESERVE AFFAIRS)
ASSISTANT SECRETARY OF THE AIR FORCE (MANPOWER AND RESERVE AFFAIRS)
COASTAL MISSISSIPPI MARKET, DEFENSE HEALTH AGENCY
JACKSONVILLE MARKET, DEFENSE HEALTH AGENCY
NATIONAL CAPITAL REGION MARKET, DEFENSE HEALTH AGENCY
CENTRAL NORTH CAROLINA MARKET, DEFENSE HEALTH AGENCY
DIRECT SUPPORT ORGANIZATION ARMY
DIRECT SUPPORT ORGANIZATION NAVY
DIRECT SUPPORT ORGANIZATION AIR FORCE

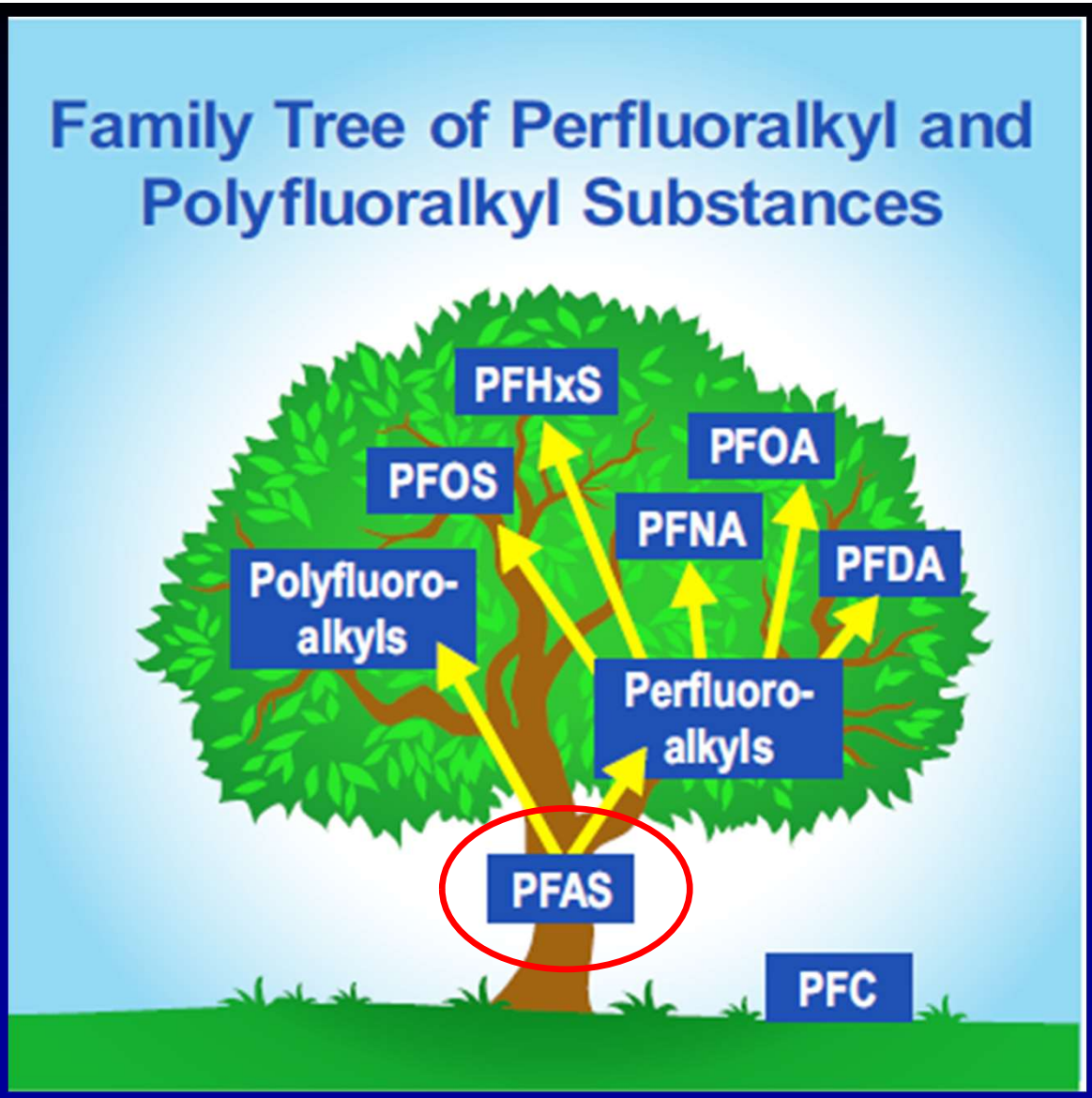
SUBJECT: Blood Testing Department of Defense Firefighters for Perfluoroalkyl and Polyfluoroalkyl Substances

The National Defense Authorization Act for Fiscal Year 2020 (NDAA FY 2020), Section 707 issues a requirement:

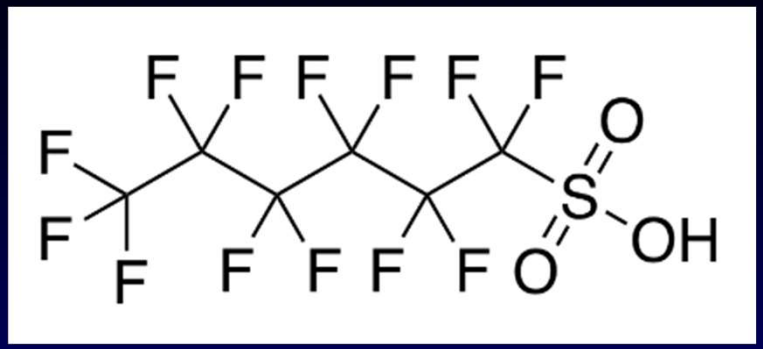
"Beginning on October 1, 2020, the Secretary of Defense shall provide blood testing to determine and document potential exposure to perfluoroalkyl and polyfluoroalkyl substances (commonly known as "PFAS") for each firefighter of the Department of Defense (DoD) during the annual physical exam conducted by the Department for each such firefighter."

As such, military medical treatment facility (MTF) staff need to be prepared to offer and collect firefighter blood samples and order the PFAS test panel. To support this effort, a website was created to provide resources and information: https://health.mil/Military-Health-Topics/Combat-Support/Public-Health/PFAS.

Family Tree of Perfluoralkyl and Polyfluoralkyl Substances



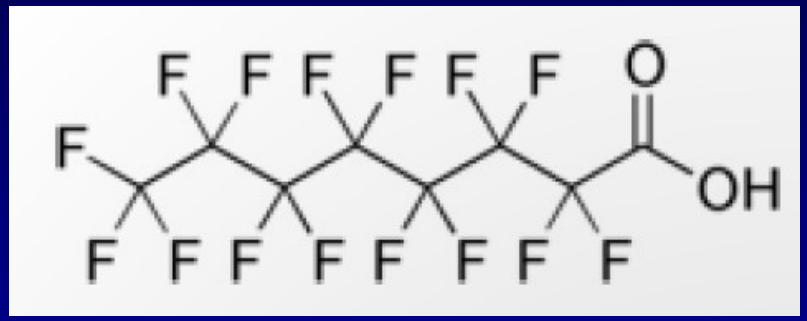
https://www.atsdr.cdc.gov
https://www.dep.pa.gov/

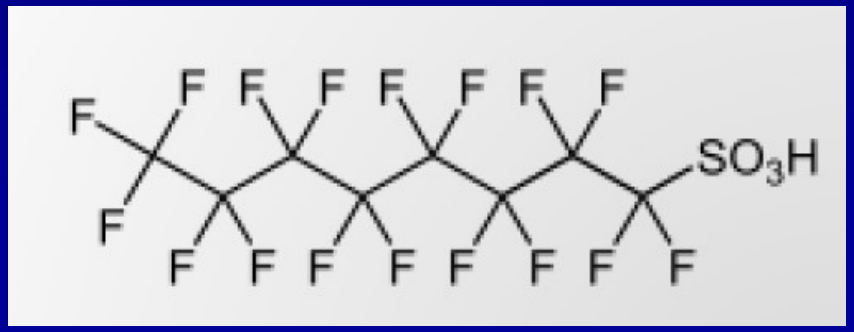


PFHxS

PFOA

aka “C8”





PFOS

Table 1. **Common PFAS: Abbreviations and Names**

Abbreviation	Chemical name
PFOS	Perfluorooctane sulfonic acid
PFOA (aka C8)	Perfluorooctanoic acid
PFNA	Perfluorononanoic acid
PFDA	Perfluorodecanoic acid
PFOSA (aka FOSA)	Perfluorooctane sulfonaminde
MeFOSAA (aka Me-PFOSA-AcOH)	2-(N-Methyl-perfluorooctane sulfonamido) acetic acid
Et-FOSAA (aka Et-PFOSA-AcOH)	2-(N-Ethyl-perfluorooctane sulfonamido acetic acid
PFHxS	Perfluorohexane sulfonic acid

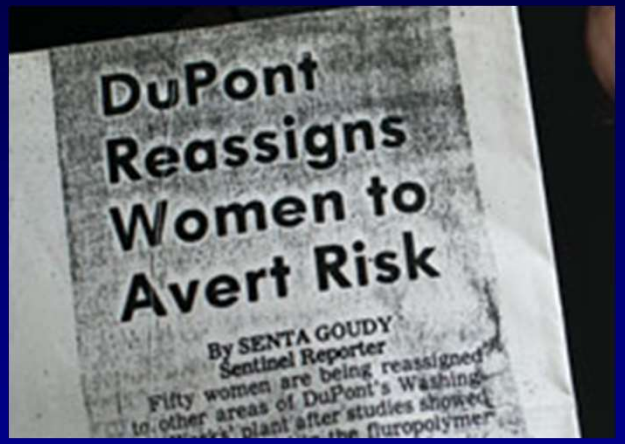
PFAS

- Uses
  - Non-stick cookware (Teflon)
  - Carpet/clothing stainproofing
  - Paper/cardboard waterproofing
  - Class B Aqueous film forming foams (AFFF) aka fire fighting foams
- Exposure Sources
  - Drinking Water
  - Dust
  - Seafood
  - Fast food
  - Produce

A (very) Brief History

1940s-1950s

1960s-1970s



1980s

A (very) Brief History

1990s-2000s

C8 Science Panel

2000s

3M Science. Applied to Life.™

2000-PFAS production ceased by 3M

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

2010s

2016 EPA LHA Recommendation

- **PFOA + PFOS <70 ppt**
- **Derived to protect fetuses and breastfed infants**
- **Lifetime advisory***
- **May reduce in 2022**

Average PFOA Water Concentrations in ppt	
C8 Study: Little Hocking, OH	3400
Hoosick Falls Municipal Water	595
C8 Study: Lubeck, WV	520
C8 Study: Tuppers Plains, OH	310

Some states choosing to go lower than EPA LHA

EPA Final Health Advisory, 2016

NYSDOH PFOA Biomonitoring Program, 2016

Toxicokinetics in Humans

- A: **ORAL** >> inhaled >> dermal
- D: Focused in **BLOOD**, liver, kidney
- M: no known in vivo metabolism
- E: **URINE** >> feces >> breast milk

CDC/ATSDR, Toxicological Profile for Perfluoroalkyls, May 2021

Estimates of elimination half-lives of representative PFAS Substances

PFOA	2.1-5-8 years
PFOS	3.1-7.4 years
PFHxS	4.7-15 years
PFBA	72-81 hours

CDC/ATSDR, Toxicological Profile for Perfluoroalkyls, May 2021

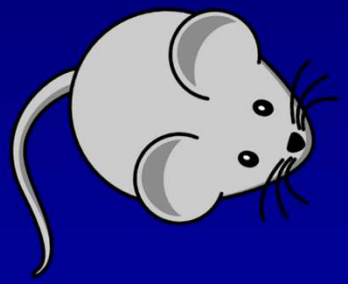
WHAT ABOUT HEALTH EFFECTS IN HUMANS?

- Primarily based on PFOA / PFOS

Epi Studies: Asks the **right** question
Examines the **right species** at the **right doses**

BUT

Answers the question poorly
Confounders/bias complicate interpretation
Not very sensitive

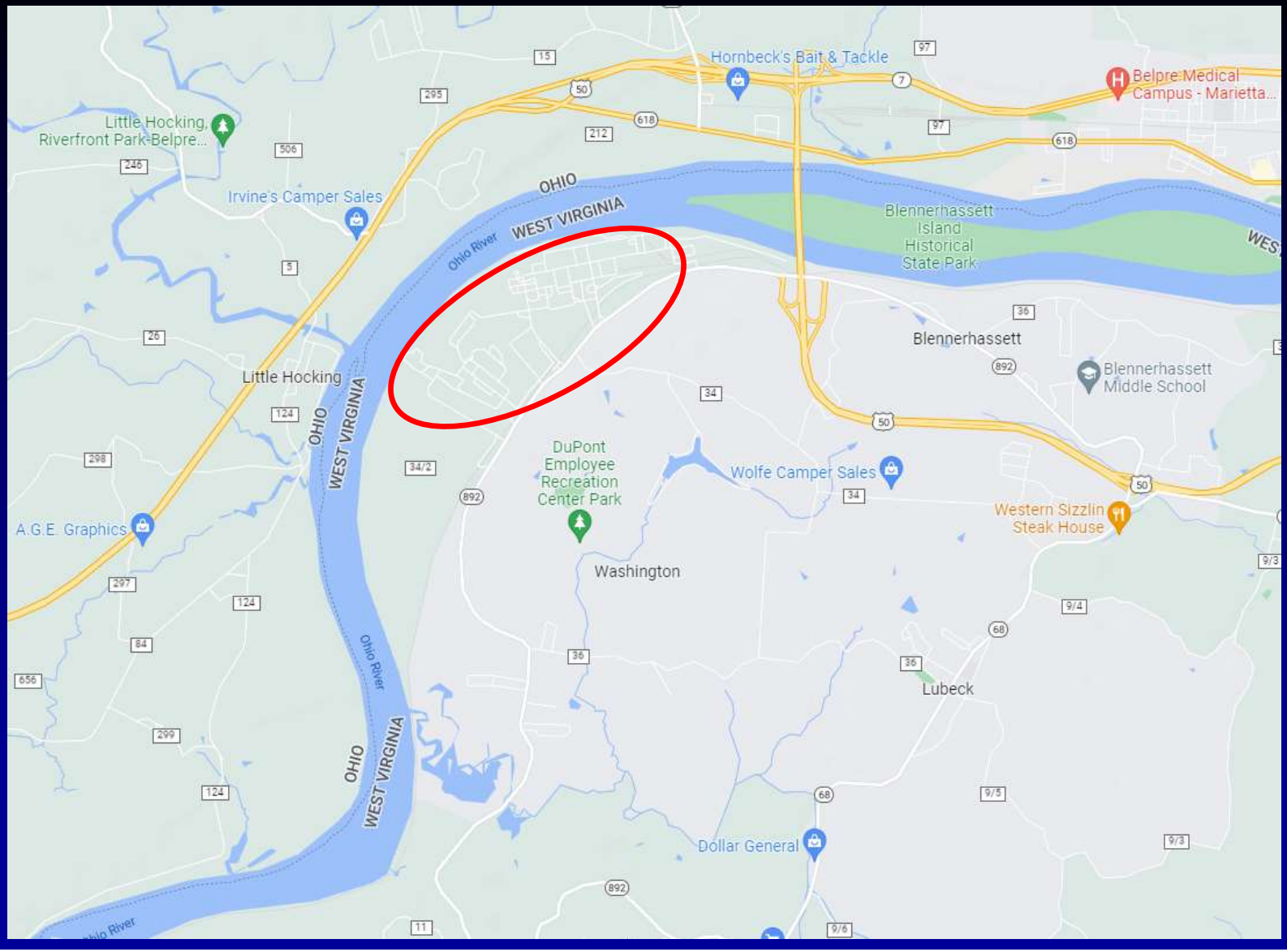


Animal Tox Studies: Asks the **wrong** question
Examines the **wrong species** at **high doses**

BUT

Answers the question well
Tight control of all variables

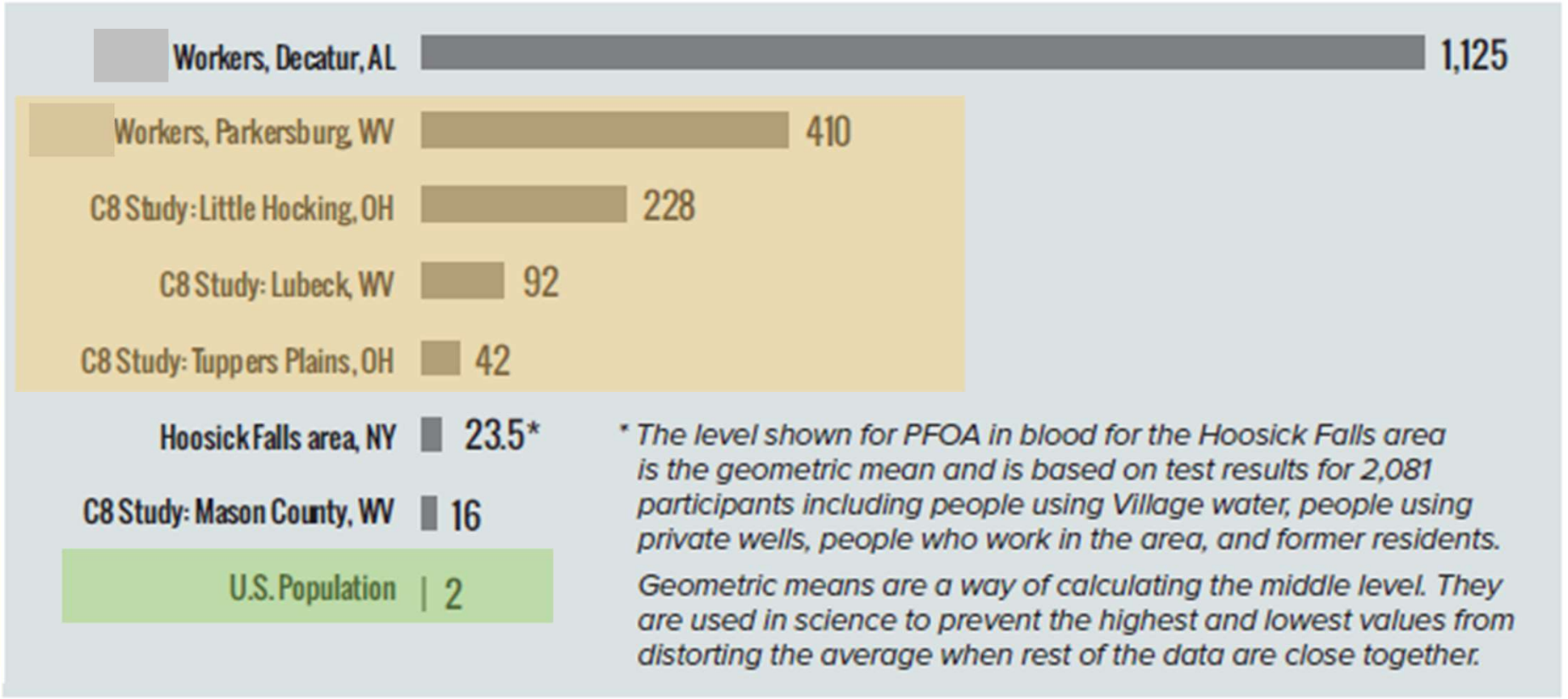
Adapted from M.E. (Bette) Meek, University of Ottawa, 2017


Hornbeck's Bait & Tackle
Belpre Medical Campus - Marietta...
Little Hocking, Riverfront Park-Belpre...
Irvine's Camper Sales
OHIO
WEST VIRGINIA
Ohio River
Blennerhassett Island Historical State Park
Blennerhassett
Blennerhassett Middle School
Little Hocking
DuPont Employee Recreation Center Park
Wolfe Camper Sales
Western Sizzlin Steak House
A.G.E. Graphics
Washington
Lubeck
Dollar General

C8 Science Panel

- Very Large Human Epi Study
- "Probable" Links
  - High cholesterol
  - Thyroid dysfunction
  - Ulcerative colitis
  - HTN of pregnancy
  - Testicular cancer
  - Kidney cancer
- Causality not confirmed
- "Probable link" → Legal Definition

Average PFOA Levels in Blood (Micrograms per Liter) Same as **ng/mL**



* *The level shown for PFOA in blood for the Hoosick Falls area is the geometric mean and is based on test results for 2,081 participants including people using Village water, people using private wells, people who work in the area, and former residents.*

Geometric means are a way of calculating the middle level. They are used in science to prevent the highest and lowest values from distorting the average when rest of the data are close together.

NHANES Data

Median Values
PFOS 19.9 ng/mL
PFOA 3.8 ng/mL

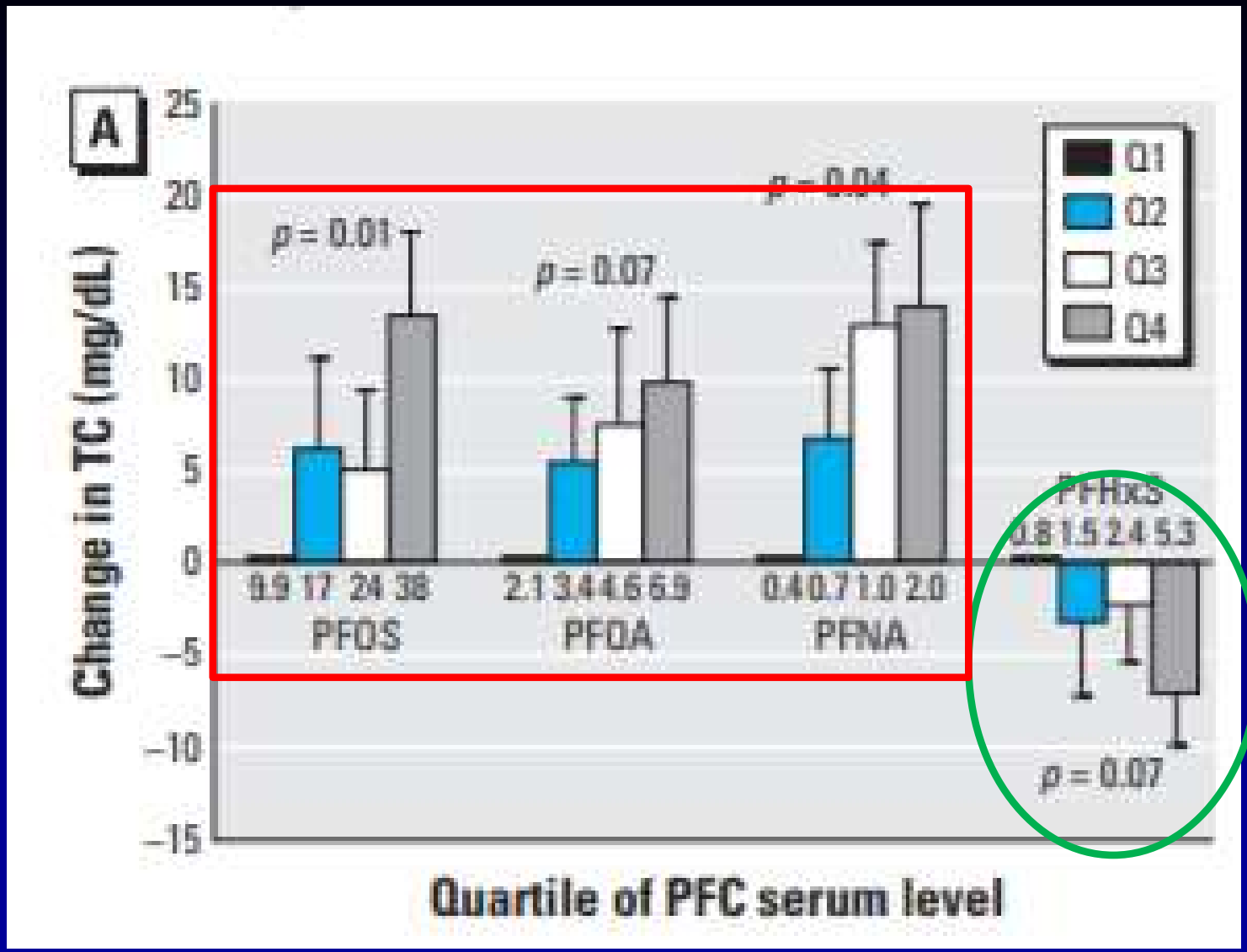


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Table 3. Overall retrospective survival analysis results based on follow-up from 1952 through 2008–2011 [RR (95%)].[a]

	Q2 vs. Q1[b]	Q3 vs. Q1	Q4 vs. Q1	p_{trend} of log cumulative exposure
Unlagged exposure				
Ulcerative colitis	1.76 (1.04, 2.99)	2.63 (1.56, 4.43)	2.86 (1.65, 4.96)	< 0.0001
Crohn's disease	1.25 (0.61, 2.58)	1.15 (0.55, 2.41)	1.00 (0.48, 2.09)	0.73
Rheumatoid arthritis	1.24 (0.85, 1.79)	1.40 (0.96, 2.03)	0.99 (0.68, 1.43)	0.84
Type 1 diabetes–broad[c]	0.68 (0.29, 1.58)	0.53 (0.22, 1.30)	0.54 (0.22, 1.33)	0.84
Type 1 diabetes–narrow[d]	0.83 (0.25, 2.78)	1.41 (0.40, 4.95)	0.88 (0.25, 3.06)	0.68
Lupus	1.49 (0.68, 3.34)	1.01 (0.44, 2.30)	0.71 (0.31, 1.65)	0.94
Multiple sclerosis	0.85 (0.44, 1.63)	1.56 (0.81, 3.00)	1.26 (0.65, 2.42)	0.22

C8 Cohort – PFOA Focus

Median PFOA Values
Community 24 ng/mL
Plant Workers 113 ng/mL

PMID: 23735465

Table 4. Associations between serum PFOA and PFOS and PIH.

PFC metric	Crude OR All births $n = 1{,}600$ (106 cases)	Adjusted[a] OR (95% CI) All births $n = 1{,}600$ (106 cases)	Adjusted[a] OR (95% CI) First prospective[b] $n = 770$ (43 cases)
PFOA			
Per in unit increase	1.18	1.27 (1.05, 1.55)	1.23 (0.92, 1.64)
Per IQR increase[c]	1.04	1.06 (0.99, 1.14)	1.04 (0.92, 1.18)
Quintile (ng/mL)		p-trend = 0.005	p-trend = 0.124
0 to < 6.9	1.0 (reference)	1.0 (reference)	1.0 (reference)
6.9 to < 11.1	2.37	2.39 (1.05, 5.46)	0.62 (0.13, 3.01)
11.1 to < 18.9	2.72	3.43 (1.50, 7.82)	2.68 (0.78, 9.23)
18.9 to < 37.2	2.71	3.12 (1.35, 7.18)	2.30 (0.66, 8.00)
≥ 37.2	2.59	3.16 (1.35, 7.38)	1.69 (0.45, 6.28)

C8 Cohort – >1,600 pregnancies

Median Values
PFOS 15.6 ng/mL (95th % 31.8 ng/mL)
PFOA 31 ng/mL (95th % 114.1 ng/mL)

PMID: 23838280

Table 5. HRs (95% CIs) by PFOA quartile[a] for thyroid, kidney, and testicular cancer cases among the cohort ($n = 32,254$).

Cancer	No. of cases[b]	Quartile 1 (reference)	Quartile 2	Quartile 3	Quartile 4	*p*-Value[c]	*p*-Value[d]
Kidney							
No lag	105	1.00	1.23 (0.70, 2.17)	1.48 (0.84, 2.60)	1.58 (0.88, 2.84)	0.18	0.10
10-year lag	105	1.00	0.99 (0.53, 1.85)	1.69 (0.93, 3.07)	1.43 (0.76, 2.69)	0.34	0.15
Testes							
No lag	17	1.00	1.04 (0.26, 4.22)	1.91 (0.47, 7.75)	3.17 (0.75, 13.45)	0.04	0.05
10-year lag	17	1.00	0.87 (0.15, 4.88)	1.08 (0.20, 5.90)	2.36 (0.41, 13.65)	0.02	0.10
Thyroid							
No lag	86	1.00	1.54 (0.77, 3.12)	1.48 (0.74, 2.93)	1.73 (0.85, 3.54)	0.25	0.20
10-year lag	86	1.00	2.06 (0.93, 4.56)	2.02 (0.90, 4.52)	1.51 (0.67, 3.39)	0.57	0.65

[a]Quartiles were defined by the estimated cumulative PFOA serum concentration among the thyroid, kidney, or testicular cancer cases at the time of cancer diagnosis. [b]A proportional hazards regression model was run for each cancer; each model was adjusted for time-varying smoking, time-varying alcohol consumption, sex, education, and stratified by 5-year period of birth year. Time began at age 20 years if the person's 20th birthday was in 1952 or later; otherwise time began at the age the person was in 1952; time ended at the age of cancer diagnosis, age at the last follow-up survey, or age on December 31st 2011, whichever came first. [c]*p*-Value is for linear trend test in the log rate ratios across quartiles; *p*-Values were calculated using exposure category midpoints and inverse variance weighting in a no-intercept linear regression model. [d]*p*-Value is from the continuous log estimated cumulative PFOA serum concentration models.

C8 Cohort – PFOA Focus

>2500 validated cancers

Median PFOA Values
Community 24 ng/mL
Plant Workers 113 ng/mL

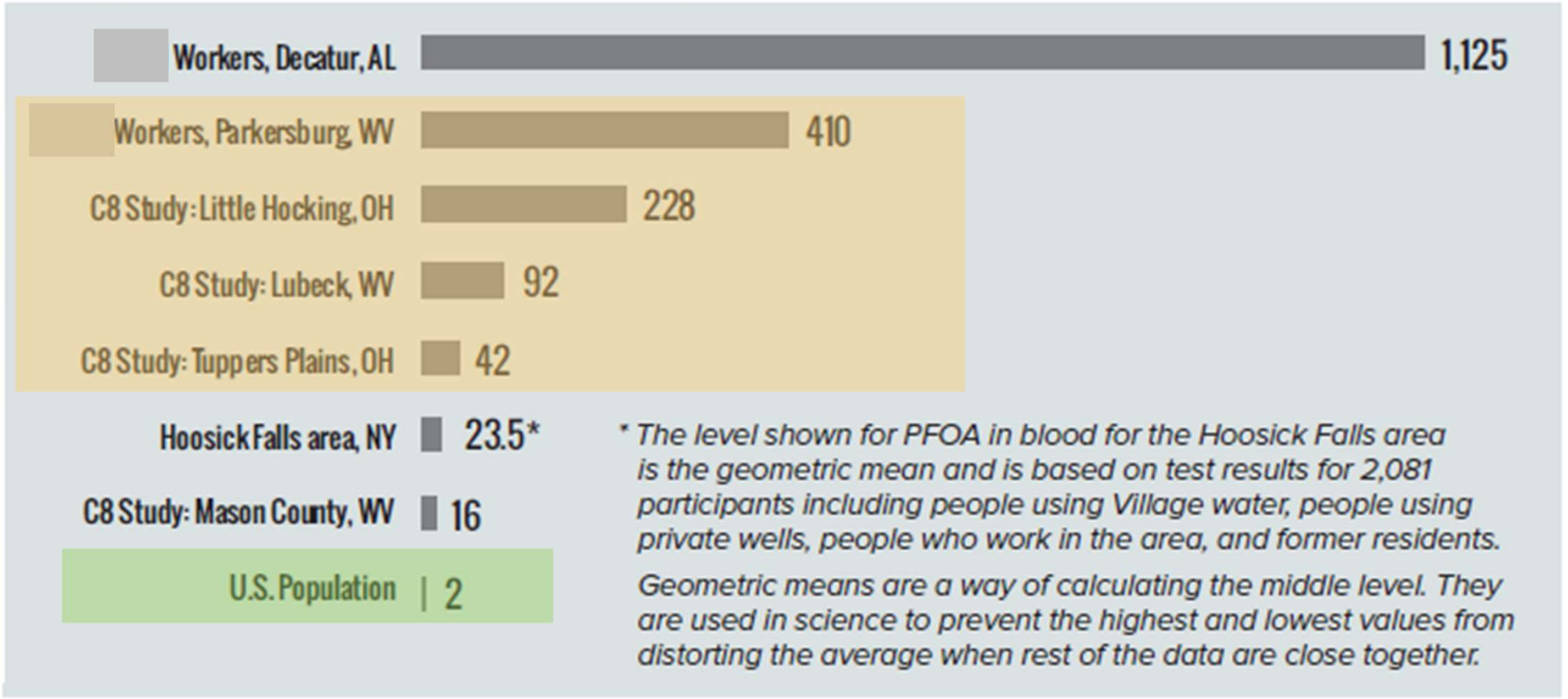
Note: "Survivor Cohort"

PMID: 24007715

Occupational Epidemiology

- PFAS plant workers
  - Outcome data
- Firefighters
  - Exposure assessments
  - No outcome data

Average PFOA Levels in Blood (Micrograms per Liter) Same as **ng/mL**



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Geometric means are a way of calculating the middle level. They are used in science to prevent the highest and lowest values from distorting the average when rest of the data are close together.

WV PFOA Plant Worker Mortality Study, 2012

- 5791 workers
- 2125 blood samples, 1979-2004
- Reviewed cancer and non-cancer deaths
- Median PFOA 580 ng/mL (Rng: 160-2880 ng/mL)

PMID: 23079607

WV PFOA Plant Worker Mortality Study

- 4th quartile of exposure vs. non-PFOA workers
  - Mesothelioma SMR 6.27 (2.0-14.6)**
  - Renal cancer SMR 2.66 (1.1-5.2)
  - Chronic kidney disease SMR 8.6 (3.4-17.7)
  - Diabetes SMR 1.9 (0.98-3.3)

PMID: 23079607


MSA

Dobraca, 2015

TABLE 4. Serum PFC Concentrations (μg/L) in FOX Firefighters, 2010 to 2011, Compared With NHANES*

Serum PFCs	Population	*n*	LOD	DF (%)	Percentiles				Maximum	Geometric Mean‡ (95% CI)
					25th	50th	75th	95th		
PFOS	FOX	101	0.083	100	10.10	12.70	16.80	24.70	46.60	12.50 (11.34, 13.78)
Perfluorooctane sulfonic acid	NHANES	876	0.2	99.8	8.30	12.30	17.60	40.40	281.0	12.13 (10.43, 14.10)
PFOA	FOX	101	0.301	100	2.96	3.86	4.89	9.54	18.10	3.75 (3.37, 4.17)
Perfluorooctanoic acid	NHANES	876	0.1	99.7	2.70	3.70	5.10	8.20	24.00	3.61 (3.28, 3.98)
PFHxS	FOX	101	0.012	100	1.61	2.27	3.13	4.64	13.20	2.26 (2.00, 2.54)
Perfluorohexane sulfonic acid	NHANES	876	0.1	99.6	1.40	2.20	3.40	6.90	44.80	2.15 (1.93, 2.40)
PFNA	FOX	101	0.075	100	0.89	1.13	1.49	2.21	4.23	1.15 (1.06, 1.25)
Perfluorononanoic acid	NHANES	876	0.082	99.8	0.98	1.31	1.89	4.18	17.95	1.40 (1.20, 1.63)
PFDeA	FOX	101	0.032	100	0.51	0.72	1.72	2.63	4.60	0.90 (0.78, 1.03)
Perfluorodecanoic acid	NHANES	876	0.1	96.4	0.20	0.30	0.40	0.90	20.70	0.30 (0.28, 0.34)

- California study
- 101 Firefighters

- Some ↑ PFHpA if Class A Foam used in last year**

PMID: 25563545

Rotander, 2015

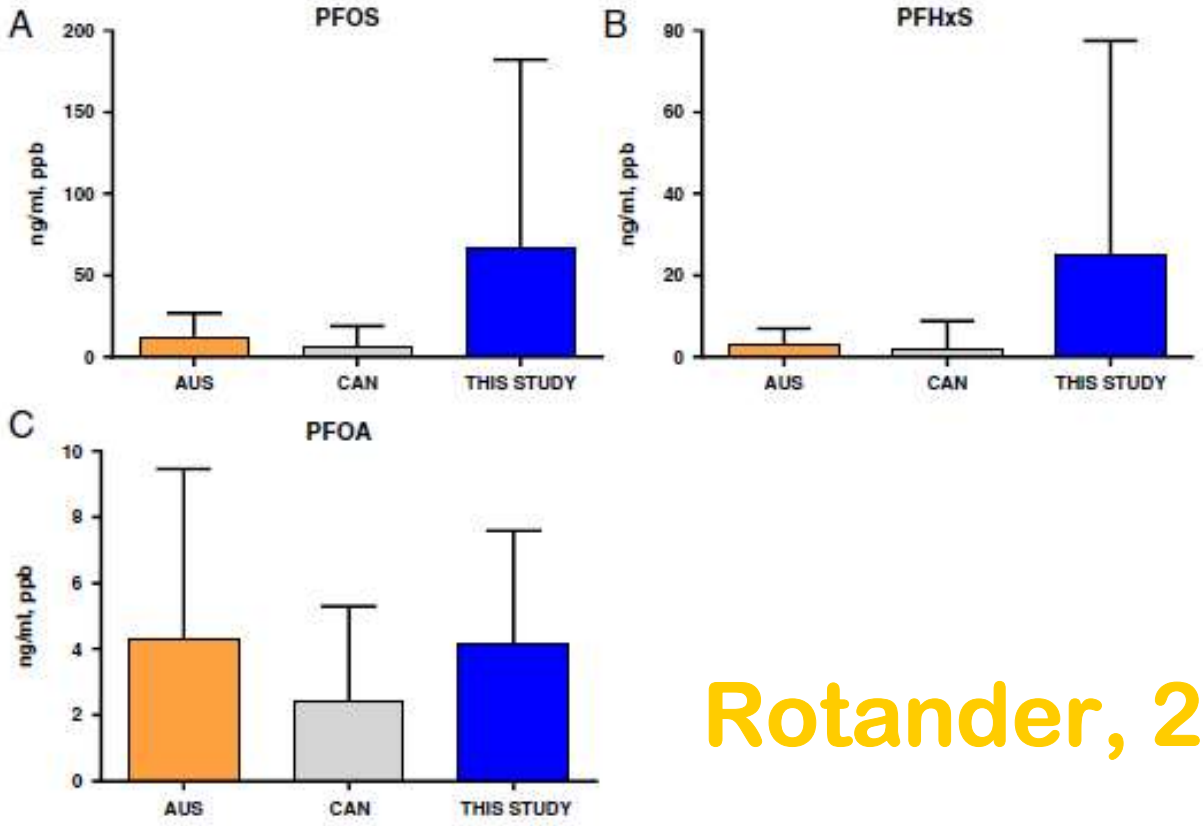
Table 1
Serum levels (ng/mL serum) of eleven PFAAs found above LOD in 149 firefighters.

Compound	% > LOD	Mean (SD)	Median	Range
Perfluorooctanesulfonic acid, PFOS	100	74 (61)	66	3.4–391
Perfluorohexanesulfonic acid, PFHxS	100	33 (36)	25	0.7–277
Perfluorooctanoic acid, PFOA	100	4.6 (2.4)	4.2	0.3–18
Perfluoroheptanoic acid, PFHpA	50	0.10 (0.08)	0.07	<0.03–0.38
Perfluorononanoic acid, PFNA	100	0.76 (0.3)	0.69	0.09–2.4
Perfluorodecanoic acid, PFDA	99	0.29 (0.13)	0.27	<0.04–0.99
Perfluoroundecanoic acid, PFUnDA	88	0.16 (0.08)	0.14	<0.06–0.58
Perfluorododecanoic acid, PFDoDA	6.6	NC	<0.05	<0.05–0.12
Perfluorotridecanoic acid, PFTrDA	7.9	NC	<0.06	<0.06–0.10
Perfluorobutanesulfonic acid, PFBS	2.6	NC	<0.02	<0.02–0.09
Perfluorodecanesulfonic acid, PFDS	3.3	NC	<0.03	<0.03–0.07

NC = not calculated due to low detection rates.

- Australian study
- Serum PFOS 6-10x ↑ than gen pop
- Serum PFOS 20x ↓ than PFOS workers
- <10 yrs of firefighting = gen pop

PMID: 26001497

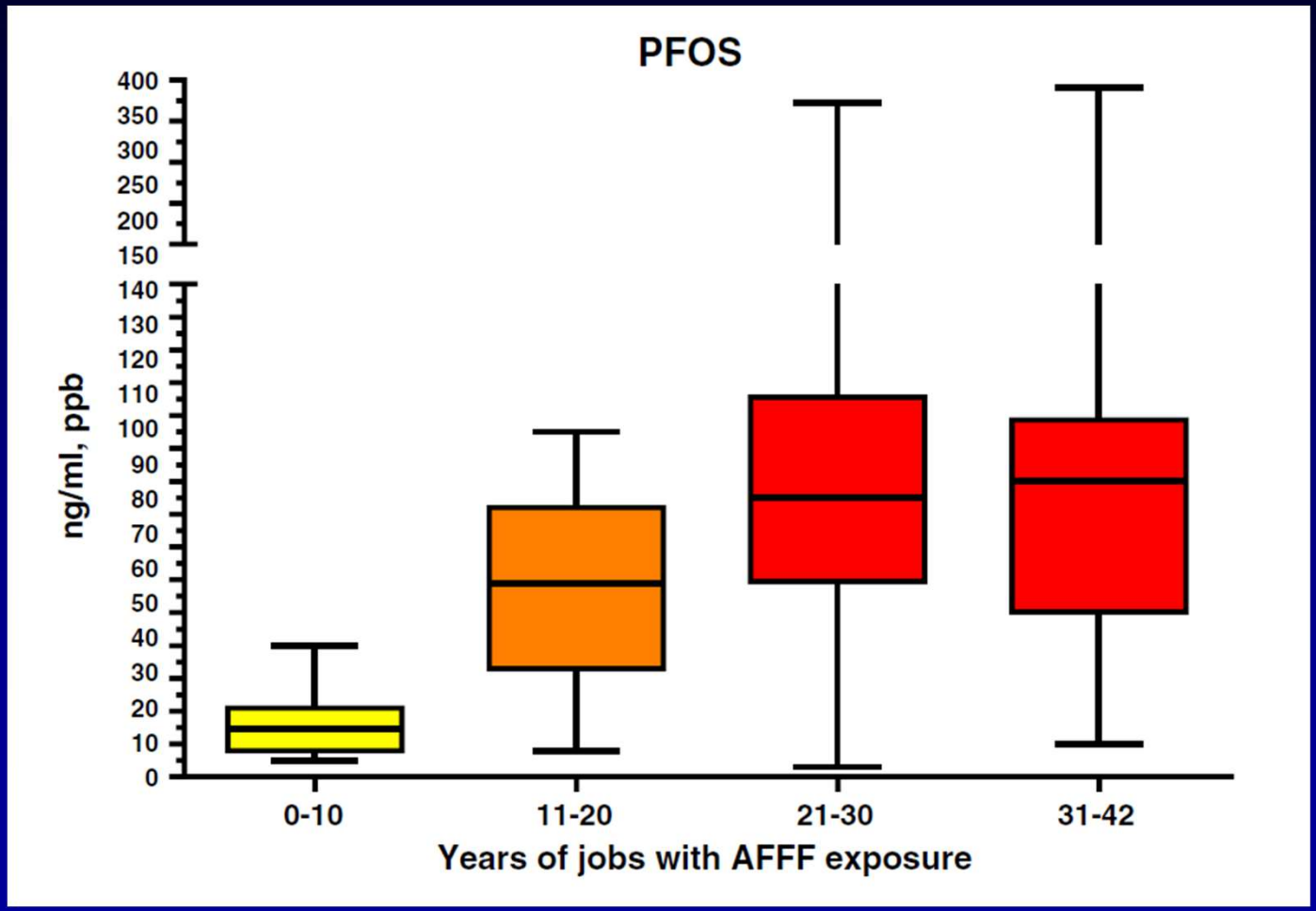


Rotander, 2015

Fig. 1. Serum concentrations (ng/mL) of A) PFOS, B) PFHxS, and C) PFOA in 16 pooled samples from Queensland, Australia (AUS), from 2010/2011 (n = 1600), and individual plasma samples from a Canadian health survey from 2010 to 2011 (n = 1016), and in this study's 149 firefighters. The whiskers indicate the 95th percentile and the columns indicate median concentrations for THIS STUDY and CAN, and mean concentrations for AUS.

PMID: 26001497

Rotander, 2015



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Graber, 2021

- 116 volunteer FF in NJ
- Compared to NHANES
- Reported less use of AFFF

	PFAS Prevalence [1]		
		NHANES	
	CAPS (n = 116)	2015–2016 (n = 274)	2017–2018 (n = 272)
Perfluorononanoic acid (PFNA)	100	98.2	92.1
Perfluorohexanesulfonic acid (PFHxS)	100	98.4	99.4
Perfluorooctanoic acid [4] (PFOA)	100	100	100
Perfluorooctanesulfonic acid [4] (PFOS)	100	100	100
2-(*N*-Methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA)	11.2	38.9	60.6
Perfluorodecanoic acid (PFDA)	99.1	69.6	89.3
Perfluoroundecanoic acid (PFUnDA)	46.6	40.8	65.5
Perfluorododecanoic acid (PFDoA)	80.1	2.4	–

PMID: 33918459

Graber, 2021

	PFAS Serum Levels (ng/mL)					
	CAPS (n = 116)		NHANES 2015–2016 (n = 274)			
	gm [2]	(95% CI) [3]	Gm [2]	(95% CI) [3]	% diff [3]	C
Perfluorononanoic acid (PFNA)	0.97	(0.89, 1.05)	0.63	(0.56, 0.70)	35.1%	
Perfluorohexanesulfonic acid (PFHxS)	1.83	(1.61, 2.09)	1.80	(1.55, 2.09)	1.6%	
Perfluorooctanoic acid [4] (PFOA)	2.07	(1.89, 2.26)	1.94	(1.76, 2.14)	6.3%	
Perfluorooctanesulfonic acid [4] (PFOS)	4.25	(3.76, 4.80)	6.76	(6.13, 7.47)	−59.1%	
2-(*N*-Methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA)	0.08	(0.07, 0.09)	0.13	(0.11, 0.14)	−62.5%	
Perfluorodecanoic acid (PFDA)	0.31	(0.29, 0.33)	0.15	(0.13, 0.17)	51.6%	
Perfluoroundecanoic acid (PFUnDA)	0.11	(0.10, 0.12)	0.10	(0.09, 0.11)	9.1%	
Perfluorododecanoic acid (PFDoA)	0.14	(0.13, 0.15)	0.07	(0.07, 0.07)	50.0%	

PMID: 33918459

Back to Our Case

- Firefighter requests information
- Perfluorohexane sulfonic acid (PFHxS)

Firefighter lab report example

Substance	Abbreviation
Perfluorobutanesulfonic Acid	PFBS
Perfluoroheptanoic Acid	PFHpA
Perfluorohexanesulfonic Acid	PFHxS
Perfluorooctanoic Acid	PFOA; FC-143 Component
Perfluorononanoic Acid	PFNA
Perfluorooctanesulfonic Acid	PFOS

Perfluorohexanesulfonic Acid	1.7	ng/mL	01

Reporting Limit: 0.050 ng/mL

Synonym(s): PFHxS

Population reference interval derived from NMS Labs data (n=151) is usually less than 5.8 ng/mL (90% CI, 4.1 - 17 ng/mL) (97.5th percentile)

General U.S. population from CDC-NHANES (2015-2016) (n=1993) (isomers not described) is typically below 4.9 ng/mL (95% CI, 4.1 - 5.8 ng/mL) (95th percentile)

Analysis by High Performance Liquid Chromatography/ Tandem Mass Spectrometry (LC-MS/MS)

Downs Thoughts

- Reassurance (at this time)
  - Outcome data specific to PFHxS is limited
- Focused clinical evaluation if warranted
  - No additional testing “just to see”
  - Standard CBC, CMP unlikely to be altered
- Human Clinical Testing for PFAS is limited
  - In both availability and utility
  - Available for firefighters only in DOD

Don’t Forget Basic OEM Practice

If We Saw an Employee With Elevated Biomarkers For Any Other Substance, What Would We Do?

CDC Now Recruiting for 'Pease Study' on Health Effects of PFAS in Drinking Water

New Hampshire Public Radio | By Annie Ropeik
Published October 25, 2019 at 11:41 AM EDT

Future Efforts

Enrollment ended Dec 2021

Expect results in 2 years

The Defense Department held its second virtual PFAS public engagement recently, the first being in July. Attendees were primarily from communities around military installations where PFAS, or per- and polyfluoroalkyl substances, have been identified in groundwater. Representatives from the White House and the Environmental Protection Agency also attended.

Future Efforts

Another talk for another day by another speaker…

Questions/Discussion

Thank you!

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