Evaluating Immunotoxicity within Washington State from Polyfluoroalkyl Contaminated Drinking Water

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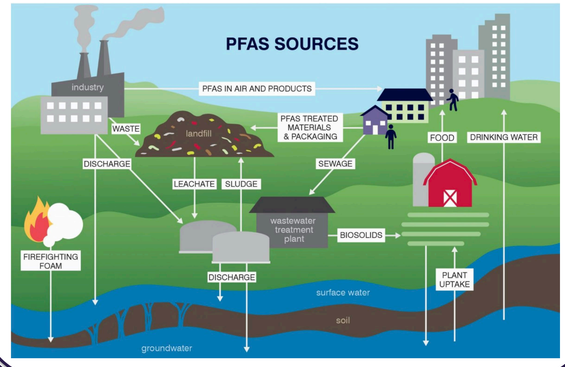
ABSTRACT

Polyfluoroalkyl substances (PFAS) are chemical pollutants that are classified as endocrine-disrupting chemical family and are used within a variety of industrial manufacturing and consumer products. PFASs easily bioaccumulate and disperse within ecosystems leading to biochemical and physiological disruptions on affected populations. Previous studies have associated PFAS's exposure with the development of immunotoxicity including immunosuppression, hypersensitivity, and autoimmunity within regions of high exposure levels. Children and adolescence appear to be the most affected with PFAS exposure as it can diminish the development of vaccine antibodies. Within Washington State, high levels of PFASs have been observed over several locations near various military bases, however evaluation of the health effects on the surroundings communities is not known. Within our research we sought to better understand the correlation between PFAS exposure rates and the development of immunotoxicity in correlating Washington State populations. We performed a comprehensive literature review that analyzed the development of immunotoxicity with various PFAS toxicity levels and then cross references this data to the know PFAS exposure rates within Washington State. We discovered the exposed populations showed significantly elevated PFAS contaminated blood serum samples which correlated to possible immunotoxicity development, as seen in previous literature. These findings raise a public health concern as exposed children may be unknowingly experiencing vaccine antibody levels below the threshold of protection, thus making exposed children are at risk for infection and transmission of diseases within their residing communities. Further biomonitoring and antibody analysis is needed in order to assess the immunotoxicity severity of affected populations.

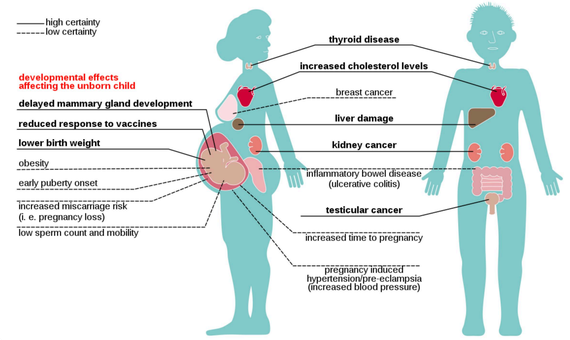
METHODS

A comprehensive literature review was preformed that analyzed immunotoxicity characteristics of PFAS chemicals in associated with blood serum concentrations. This was then cross referenced with the reported data within Washington State of PFAS exposure. An extensive analysis of governmental reports was included within this literature review.

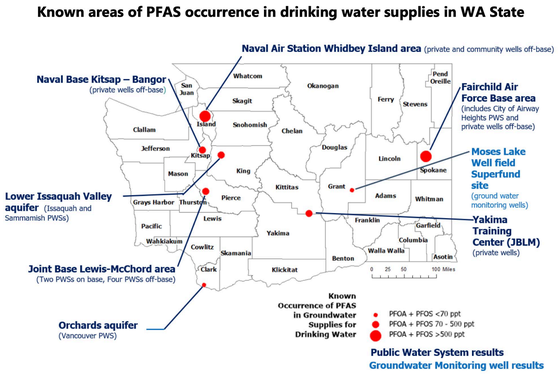
LIFECYCLE OF PFASs

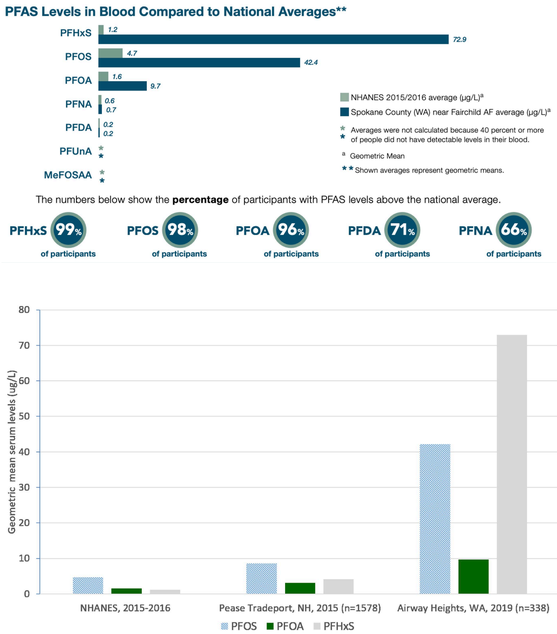


PFASs HEALTH EFFECTS



PFASs CONCENTRATIONS FROM RESIDENTS IN SPOKANE, WA



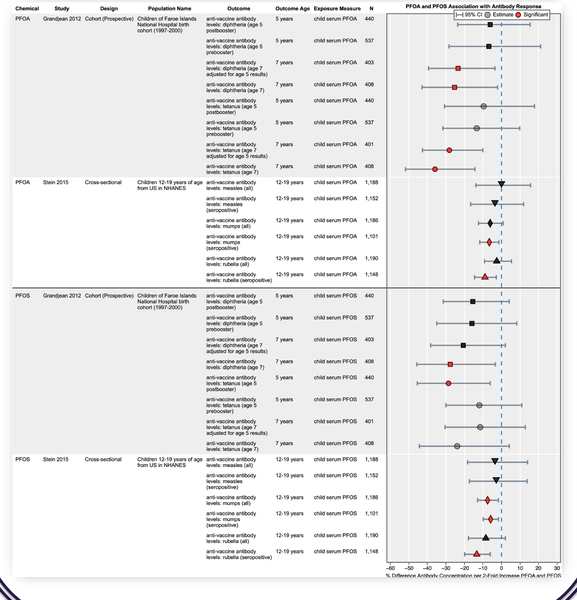


➢ PFAS blood serum samples in Spokane, WA compared to national average and New Hampshire.

IMMUNOSUPPRESSION

Table 11. Summary of PFOA/PFOS and Selected Data on Antibody Response in Humans

Vaccine	Change in antibodies with PFOA[a]	Change in antibodies with PFOS[a]	Possible sources of heterogeneity	Exposure measure timing	Study
Rubella	**-0.4 (-0.64 to -0.17)**	**-0.08 (-0.14 to -0.02)**	• developmental exposure metric	Maternal 0-3d post delivery	Granum (2013)
	-8.9 (-14.6 to -2.9)	**-13.3 (-19.9 to -6.2)**	• childhood exposure metric • booster vaccination	Children: current	Stein (2016)
Diphtheria	**-22.8 (-39.4 to -1.7)**	-19.7 (-41.8 to 10.7)	• developmental exposure metric • antibody levels measured at age 7	Maternal week 32 gestation	Grandjean (2012)
	-25.2 (-42.9 to -2.0)	**-27.6 (-45.8 to -3.3)**	• childhood exposure metric • antibody levels measured at age 7	Children (age 5)	Grandjean (2012)
	OR = 3.27 (1.43 to 7.51)	**OR = 2.38 (0.89 to 6.35)**	• outcome is OR of falling below protective level of 0.1 IU/ml) • childhood exposure metric • antibody levels measured at age 7	Children (age 5)	Grandjean (2012)
	-8.2 (-20.8 to 6.4)	**-11.9 (-21.9 to -0.3)**	• outcome is antibody rise not levels • outcome in adults	Adults 10-days post vaccination	Kielsen (2016)
Mumps	**-6.6 (-11.7 to -1.5)**	**-5.9 (-9.9 to -1.6)**	• childhood exposure metric • booster vaccination	Children: current	Stein (2016)
Measles	-0.13 (-0.35 to 0.09)	-0.05 (-0.1 to 0.01)	• developmental exposure metric	Maternal 0-3d post delivery	Granum (2013)
	-3.4 (-16.7 to 11.9)	-2.9 (-17.3 to 13.9)	• childhood exposure metric • booster vaccination	Children: current	Stein (2016)
Tetanus	-0.01 (-0.09 to 0.1)	-0.002 (-0.03 to 0.02)	• developmental exposure metric	Maternal 0-3d post delivery	Granum (2013)
	7.4 (-17.1 to 39.0)	35.3 (-3.9 to 90.6)	• developmental exposure metric • antibody levels measured at age 7	Maternal week 32 gestation	Grandjean (2012)
	-35.8 (-51.9 to -14.2)	-23.8 (-44.3 to 4.2)	• childhood exposure metric • antibody levels measured at age 7	Children (age 5)	Grandjean (2012)
	OR = 4.20 (1.54 to 11.44)	**OR = 2.61 (0.77 to 8.92)**	• outcome is OR of falling below protective level of 0.1 IU/ml) • childhood exposure metric • antibody levels measured at age 7	Children (age 5)	Grandjean (2012)
	0.23 (-10.4 to 12.1)	-3.6 (-11.9 to 5.5)	• outcome is antibody rise not levels • outcome in adults	Adult 10-days post vaccination	Kielsen (2016)
Influenza A H3N2	**Antibody titer ratio** 2nd -0.1 (-0.3 to 0.1) 3rd -0.07 (-0.28 to -0.14) **4th -0.22 (-0.43 to -0.01)**	**Antibody titer ratio** 2nd -0.06 (-0.26 to 0.14) 3rd -0.02 (-0.18 to -0.23) 4th -0.03 (-0.24 to -0.19)	• outcome is antibody rise not levels • outcome in adults	Adult at vaccination	Looker (2014)
	Antibody titer rise **2nd -0.28 (-0.51 to -0.06)** **3rd -0.37 (-0.60 to -0.13)** 4th -0.12 (-0.36 to 0.13)	**Antibody titer rise** 2nd 0.03 (-0.19 to 0.26) 3rd 0.18 (-0.00 to 0.41) 4th -0.04 (-0.28 to 0.21)			

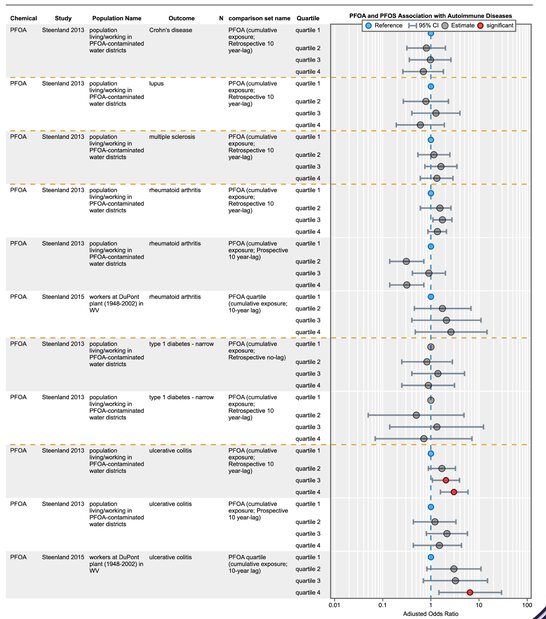


HYPERSENSITIVITY

Table 16. Summary of PFOA and Selected Data on Hypersensitivity in Humans

Disease	PFOA	Possible sources of heterogeneity	Exposure measurement	Study
Asthma	Adj OR (95% CI) 4th vs. lowest quartile **OR = 4.05 (2.21 – 7.42)** 3rd vs. lowest quartile **OR = 2.67 (1.49 – 4.79)** **Trend p<0.001 (males + females)**	• ever asthma • childhood exposure metric • sig. for males, females, combined	Child: current serum	Dong (2013) and Zhu (2016)
	OR = 3.56 (0.84 – 15.02)	• ever asthma or current • maternal exposure metric	Maternal plasma 0-3d post delivery	Granum (2013)
	Adj OR (95% CI) Ln-linear or linear **p=0.04** **OR = 1.18 (1.01 – 1.39)**	• ever asthma • not sig. for current asthma • childhood exposure metric	Child: current serum	Humblet (2014)
	OR for 1 SD change in serum PFOA OR = 0.93 (0.47 – 1.84)	• current asthma • maternal exposure metric	Maternal: serum	Smit (2015)
	Disease-specific Cox regression not significant **Trend: p=0.05 for inverse association with PFOA exposure via categories**	• adult modeled exposure • not sig. lagged exposure • not sig. cumulative exposure	Adult: modeled	Steenland (2015)
Total IgE	Adj OR log10 PFOA concentration OR = 1.1 (0.6 – 1.9)	• cord blood IgE measure • maternal exposure metric	Maternal: first trimester plasma	Ashley-Martin (2015)
	Mean IgE (95% CI) quartiles PFOA in asthmatics Q1: 512.1 (329.4 – 694.8) Q2: 604.6 (422.1 – 787.1) Q3: 788.2 (274.6 – 537.9) **Q4: 836.4 (652.0 – 1020.8)** **Trend: p=0.005 (males + females)**	• childhood exposure metric • childhood IgE measure • outcome in asthmatics • not sig. in non-asthmatics • sig for females, combined, not males (p trend=0.100)	Total IgE in serum in children (age 12-19)	Dong (2013) and Zhu (2016)
	Log10 quadratic PFOA quadratic polynomial regression coefficient **F: -1.429 (-2.416 – -0.0422)** **M:** 0.227 (-1.584 – 2.037)	• maternal exposure metric • cord blood IgE measure	Maternal serum after the second trimester of pregnancy	Okada (2012)
	Adj % change (95% CI) for doubling of PFOA: **OR = 10.5 (0.17 – 22)**	• childhood exposure metric	Child: Current serum	Stein (2016)
	Adjusted β (S.E.) **β =0.134 (0.115), p=0.047** F: β =0.067 (0.231), p=0.823 **M: β=0.206 (0.165), p=0.025**	• cord exposure metric • cord blood IgE measure • not sig. in childhood IgE measure	Cord blood serum sample measures of PFOA/PFOS (ng/ml)	Wang (2011)
Rhinitis	Adj OR for shift from 25th to 75th percentile (95% CI) of PFOA: **OR = 1.35 (1.10 – 1.66)**	• childhood exposure metric	Child: Current serum	Stein (2016)

AUTOIMMUNITY



PRELIMINARY CONCLUSIONS

- ➢ PFAS blood serum samples from residents within Spokane, WA show elevated levels compared to national average.
- ➢ Blood serum levels were notably higher compared to previous literature studies.
- ➢ Elevated blood serum samples compared to controlled studies would implicate immunotoxicity effects for affected residents
- ➢ Further biomonitoring is needed to assess for immunotoxicity effects
- ➢ Residents from remaining contaminated sites within Washington need to be tested and analyzed.