Environmental Pollution 246 (2019) 482–490

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Cord blood perfluoroalkyl substances in mothers exposed to the World Trade Center disaster during pregnancy☆

Miranda J. Spratlen [a, b, *], Frederica P. Perera [a], Sally Ann Lederman [c], Morgan Robinson [d], Kurunthachalam Kannan [d, e], Leonardo Trasande [f, g, h, 1], Julie Herbstman [a, 1]

[a] Columbia Center for Children's Environmental Health, Department of Environmental Health Sciences, Columbia University Mailman School of Public Health, New York, NY, USA
[b] Department of Environmental Health & Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[c] Department of Population and Family Health, Columbia University Mailman School of Public Health, New York, NY, USA
[d] Wadsworth Center, New York State Department of Health, Albany, NY, USA
[e] Department of Environmental Health Sciences, School of Public Health, State University of New York at Albany, Albany, NY, USA
[f] Department of Pediatrics, New York University School of Medicine, New York, NY, USA
[g] Department of Environmental Medicine, New York University School of Medicine, New York, NY, USA
[h] Department of Population Health, New York University School of Medicine, New York, NY, USA

ARTICLE INFO

Article history:
Received 14 September 2018
Received in revised form
7 December 2018
Accepted 7 December 2018
Available online 11 December 2018

Keywords:
Perfluoroalkyl substances
Cord blood
World Trade Center disaster

ABSTRACT

Perfluoroalkyl substances (PFAS) may have been released during the collapse of the World Trade Center (WTC) on 9/11. Evidence suggests PFAS can cross the placental barrier in humans and cause harm to the developing fetus; however, no studies have measured PFAS in mothers exposed to the WTC disaster during pregnancy. We measured PFAS in maternal plasma (n = 48) or cord blood (n = 231) from pregnant women in the Columbia University WTC birth cohort, enrolled between December 13, 2001 and June 26, 2002 at one of three hospitals located near the WTC site. In order to maximize sample size, we used a linear regression to transform the 48 maternal plasma samples to cord blood equivalents in our study; cord blood and transformed maternal plasma-to-cord blood samples were then analyzed together. We evaluated the association between WTC exposure and PFAS concentrations using three exposure variables: 1) living/working within two miles of WTC; 2) living within two miles of WTC regardless of work location; and 3) working but not living within two miles of WTC. Exposure was compared with those not living/working within two miles of WTC (reference group). Living/working within two miles of WTC was associated with 13% higher perfluorooctanoic acid (PFOA) concentrations compared with the reference group [GMR (95% CI): 1.13 (1.01, 1.27)]. The association was stronger when comparing only those who lived within two miles of WTC to the reference group [GMR (95% CI): 1.17 (1.03, 1.33)], regardless of work location. Our results provide evidence that exposure to the WTC disaster during pregnancy resulted in increases in PFAS concentrations, specifically PFOA. This work identifies a potentially vulnerable and overlooked population, children exposed to the WTC disaster in utero, and highlights the importance of future longitudinal studies in this cohort to investigate later life effects resulting from these early life exposures.

1. Introduction

It has been nearly two decades since the World Trade Center (WTC) disaster, yet questions remain regarding the health of those exposed to the dust, smoke and fumes caused by the collapse, as well as persistent fires that burned for over three months following the event. In addition to WTC responders, these concerns extend to the health of residents in lower Manhattan, particularly vulnerable populations such as pregnant women. The WTC plume was comprised of thousands of tons of toxic chemicals, many of which have been shown to adversely affect the fetus, including lead, particulate matter and numerous persistent organic pollutants

☆ This paper has been recommended for acceptance by Dr. David Carpenter.

* Corresponding author. Department of Environmental Health Sciences Columbia University, 122 W168th, Room 1105, New York, NY, 10032, USA.
E-mail address: mjs2376@cumc.columbia.edu (M.J. Spratlen).

[1] Co-last authors.

https://doi.org/10.1016/j.envpol.2018.12.018
0269-7491/

(POPs) (Landrigan et al., 2004). Perfluoroalkyl substances (PFAS) were among various elevated POPs reported in personnel responding to the WTC disaster compared to nationally representative samples (Tao et al., 2008). Further, a recent study reported higher PFAS in WTC-exposed children compared to a matched comparison group, providing evidence for WTC-related residential PFAS exposures (Trasande et al., 2017).

PFAS are a synthetic subgroup of organic compounds known for their oil and water repelling properties; these qualities have led to their widespread use as surfactants and stain-resistant coatings on numerous products, including carpets, food packaging, textiles, leather, cleaning products, pesticides, non-stick cookware and notably, in fire-fighting foam (Technical Fact Sheet, 2017). Due to their persistence in the environment and human health concerns, efforts have been made to reduce production of the two most widely used PFAS, perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) (Technical Fact Sheet, 2017). In 2002, the main PFOS manufacturer in the US voluntarily phased out PFOS production and in 2006, eight major PFAS companies joined a global stewardship program aimed at eliminating PFOA emissions (Technical Fact Sheet, 2017). Still, exposure to these compounds continues to be a pertinent public health issue as measurements of PFAS in humans remain at levels that have been associated with adverse health effects, including increases in lipids and in liver enzymes, as well as cancer, immune suppression and thyroid disorders (Water, 2016a; Water, 2016b). Further, studies have shown PFAS can cross the placental barrier in humans and have been associated with reductions in fetal growth (Olsen et al., 2009; Bach et al., 2015). Despite this, few studies have evaluated levels of PFAS in cord blood; just two of which were conducted in a US population (Apelberg et al., 2007a; Kato et al., 2014). In this study, we analyzed four PFAS [PFOS, PFOA, perfluorohexanesulfonic acid (PFHxS) and perfluorononanoic acid (PFNA)] in the cord blood of a population at risk for high exposure to PFAS: women residing in lower Manhattan during and following the WTC disaster when fires continued to burn, releasing large quantities of toxic chemicals. We attempt to better understand the contribution of the WTC disaster to PFAS levels by evaluating their association with WTC exposure. Further, we add to the limited research characterizing trends in cord blood PFAS levels across sociodemographic subgroups in the US.

2. Material and methods

2.1. Study population

Data for this work came from a Columbia University birth cohort designed to study the effects of WTC exposures on pregnancy outcomes and development. Detailed methods have been described previously (Lederman et al., 2004). Briefly, 329 women with singleton pregnancies were enrolled between December 13, 2001 and June 26, 2002 at one of three hospitals located near the WTC site: Beth Israel, St. Vincent's, and New York University Downtown. Eligibility requirements included: ages between 18 and 39 years, had not smoked (>1 cigarette/at any time) during pregnancy, and self-report of no diabetes, hypertension, HIV infection or AIDS, and no use of illegal drugs in the last year. Participants provided at least one blood sample (maternal blood at the time of delivery and/or cord blood), access to their medical record and their newborn's medical record, and completion of a 30- to 45-min interview after delivery. Participants missing data on PFAS concentrations in either cord blood or maternal plasma (n = 27), race (n = 19), body mass index (BMI) (n = 3) and parity (n = 1) were excluded, resulting in a sample size of 279 participants for analyses (Fig. 1).

2.2. Sociodemographic and exposure variables

The postpartum interview was administered at the hospital in the woman's preferred or native language (English, Spanish, or Chinese). Information on maternal education, date of birth, race, parity, marital status, home smoking exposure and residential and work addresses was elicited through the questionnaire. Residential and work addresses (for the 4 weeks starting on and following 9/11) were geocoded at the Center for International Earth Science Information Network of Columbia University's Earth Institute, using geographic information system (GIS) software from Environmental Systems Research Institute (Redlands, CA), including ArcGIS 8.3 and the Street Map 2003 extension (Lederman et al., 2004). Using these data, multiple exposure categories were created: 1) women who lived within 2 miles of the WTC site regardless of where they worked; 2) women who worked but did not live within 2 miles of the WTC site; 3) women that lived or worked within 2 miles of the WTC site; and 4) women that neither worked nor lived within 2 miles of the WTC site (reference group). Two miles was selected to delineate the exposure radius based on previous findings of an association between this exposure group and birth outcomes (Lederman et al., 2004); as well as for consistency with the World Trade Center Health Registry definition of the WTC disaster area, which includes the area of Manhattan south of Houston Street and any block of Brooklyn that is within a 1.5-mile radius of the former World Trade Center site (Your 9/11 Health Care., 2018). Maternal pre-pregnancy BMI was calculated using weight in kilograms divided by height in meters squared, both abstracted from participants' medical chart. In the case of missing height (n = 36) or weight (n = 49) from the medical record, self-reported information on these variables from the hospital interview were used. Child sex and date of birth were abstracted from child's medical record. Gestational age in days was also abstracted from the medical record (if missing (n = 15), date of last menstrual period from interview minus child's date of birth was used). Gestational age on 9/11, used to determine trimester during the WTC disaster, was created by subtracting days since the 9/11 disaster on child's date of birth from child's gestational age in days at birth. Mothers were classified as being in their first trimester on 9/11 if their child had a gestational age of ≤91 days on 9/11, and in their second or third trimester if their child had a gestational age >91 days. 18 participants were not pregnant yet on 9/11 but still included in the study in the first trimester group, as exposures to the disaster persisted for months following the initial collapse. Maternal age at delivery was determined by subtracting the child's date of birth from the mother's date of birth.

2.3. PFAS measurements

Twelve PFAS [PFOS; PFOA; perfluorobutanesulfonic acid (PFBS); perfluorohexane sulfonate (PFHxS); perfluorodecanesulfonate (PFDS); perfluorooctane sulfonamide (PFOSA); perfluorohexanoic acid (PFHxA); perfluoroheptanoic acid (PFHpA); perfluorodecanoic acid (PFDA); perfluoroundecanoic (PFUnDA), perfluorododecanoate (PFDoDA) and perfluorononanoic acid (PFNA)] were measured in maternal plasma (n = 48) and cord blood (n = 231) using a solid phase extraction (SPE) procedure and high-performance liquid chromatograph interfaced with an electrospray tandem mass spectrometer at the New York State Department of Health Wadsworth Center Laboratory, using methods similar to prior studies (Kannan et al., 2004; Taniyasu et al., 2005). Internal standards for 13 C-labeled PFAS were added into plasma samples prior to the addition of reagents for extraction (Sakr et al., 2007). Solvents and method blanks (blinded to the laboratory) were tested for the presence of the PFAS. Target chemicals were not found in

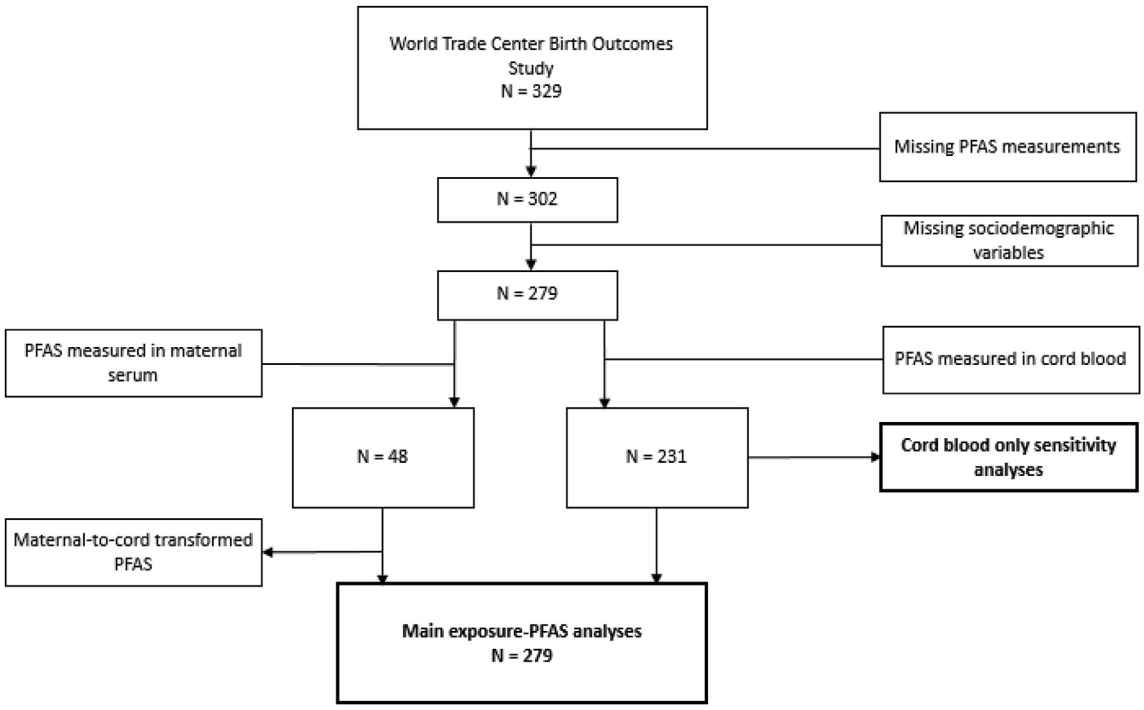

Fig. 1. Study Flow Diagram. Abbreviations: Perfluroalkyl substances (PFAS).

procedural blanks at concentrations above the limits of quantification (LOQs). The LOQs of target chemicals ranged from 0.08 to 0.20 ng/mL. A standard reference material from the National Institute of Standards and Technology (NIST) was analyzed with every batch of 50 samples and recoveries of target chemicals were between 90% and 115% of the certified values. Recoveries of target chemicals passed through the entire analytical procedure ranged between 100% and 124%. Quantification was by isotope dilution and target chemicals were monitored by multiple reaction monitoring mode under negative ionization.

2.4. Statistical analyses

All statistical analyses were conducted in R software (version 3.5.1; R Project for Statistical Computing). PFAS assessment was restricted to compounds quantified in ≥50% of samples (PFOS, PFOA, PFNA, PFHxS and PFDS). To maximize sample size, we used both maternal plasma and cord blood concentrations in analyses. However, to account for differences in maternal versus cord blood samples, we used 78 paired cord blood and maternal plasma PFAS samples from a US-based cohort with comparable PFAS concentrations, the HOME study (Apelberg et al., 2007a), to create cord blood concentration predictions from our 48 maternal samples. We were unable to create prediction models from our own data because we did not have paired samples. Separate prediction models were run for PFOS, PFOA, PFNA and PFHxS (Supplemental Table 1). Prediction models were not available for PFDS because this compound was not measured in the HOME study and was therefore not included in the main analyses for this study despite being detected in >50% of samples. Exploratory analyses evaluating PFDS only in cord blood revealed no significant associations with the WTC exposure variables (data not shown). To maximize sample size, all analyses report concentrations and associations using both transformed maternal plasma and cord blood concentrations together. PFOS, PFOA, PFNA and PFHxS were log-transformed to account for right-skewed distributions. Both PFOA and PFOS were detected in 100% of samples. Two samples (<1%) were below the LOQ (0.08 ng/mL) for PFHxS and 40 samples (14%) were below the LOQ (0.20 ng/mL) for PFNA. In accord with published practices (Kataria et al., 2015), samples < LOQ were imputed as the LOQ divided by $\sqrt{2}$.

Sociodemographic variables were compared in the final analysis dataset versus the overall dataset. Spearman correlations between log-transformed PFAS variables were explored using a correlation matrix. PFAS levels in their original scale were compared across sociodemographic variable subgroups using Kruskal-Wallis tests for subgroups with greater than two categories [race (Black, White, Asian, Other); maternal pre-pregnancy BMI (underweight: BMI<18.5 kg/m^2, normal: BMI≥18.5 & <25 kg/m^2, overweight/obese: BMI≥25 kg/m^2); education (<high school degree, high school degree, > high school degree)], and using Mann-Whitney U tests for subgroups with two categories [maternal age (<30, ≥30); child sex; trimester on 9/11 (≤91 days, >91 days); home smoking exposure (no reported smoking in household, any reported smoking in household); marital status (not married, married); and parity (primiparous, multiparous)]. Results were displayed using forest plots.

Linear regression models were used to evaluate the association between WTC exposure variables and log-transformed PFAS concentrations. The first exposure variable ("Home or Work") categorized exposed participants (n = 120) as those that either lived or worked within 2 miles of the WTC site. Participants that did not live or work within 2 miles of the disaster were categorized as the reference group (n = 159). The second exposure variable ("Home *versus* Work") attempted to better understand the contribution of home versus work exposures in PFAS levels. This exposure variable partitioned the exposed group in the "Home or Work" variable into 2 subgroups: 1) those that lived within 2 miles of the WTC site regardless of where they worked (n = 75); and 2) those that worked but did not live within 2 miles of the WTC site (n = 45). The unexposed group remained the same as the previous exposure variable, and included those that did not live or work within 2 miles

of the site (n = 159). Models report log-unit changes in PFAS concentrations by exposure category; results are exponentiated and therefore reflect geometric mean ratios (GMRs). Model 1 was unadjusted. Model 2 was adjusted for sociodemographic variables previously associated with PFAS exposure including: child sex; maternal age, education, BMI, marital status and parity; trimester pregnant during the 9/11 disaster and home smoking exposure. Model 3 further adjusted for maternal race.

To confirm findings, several sensitivity analyses were conducted. First, we ran analyses using just PFAS concentrations measured in cord blood (n = 231) to evaluate consistency with analyses using maternal-to-cord transformed concentrations. Second, to check whether using a complete case analysis biased our analyses, we also ran analyses filling in missing values in our covariates using multiple imputation using Fully Conditional Specification (FCS) implemented by the MICE (multivariate imputation by chained equations) algorithm. Analyses were conducted using the "MICE" r package with the number of imputed datasets set to 10. Finally, among a subset of participants (n = 165) with information on local fish intake, we ran analyses additionally adjusting for this variable to better understand whether other sites of PFAS contamination (e.g, contaminated waterways, and in turn contaminated local fish) might confound associations.

3. Results

3.1. Participant characteristics

Cord blood PFAS geometric means were generally lower than maternal plasma concentrations (Table 1). Our maternal-to-cord transformed concentrations plus cord blood concentrations together were slightly lower than cord blood concentrations alone. Geometric mean (range) concentrations of PFAS variables (cord blood plus maternal-to-cord transformed) were 6.03 (1.05, 33.7) ng/ml for PFOS, 2.31 (0.18, 8.14) ng/ml for PFOA, 0.43 (<LOQ, 10.3) ng/ml for PFNA and 0.67 (<LOQ, 15.8) ng/ml for PFHxS (Table 1). All PFAS variables were significantly correlated ($p = <0.01$) with each other. Correlations ranged from 0.17 between PFOA and PFNA and 0.70 between PFNA and PFOS (Fig. 2). Median (interquartile range (IQR)) age of the study population was 31.0 (27.3–34.6) years (Table 2). Roughly half of newborns were female (52.3%); 43.7% of the population was White, 36.2% were Asian, 16.1% were Black and 3.9% reported a race not defined by the previous categories. The majority of participants had a normal BMI (72%), with 18.6% overweight/obese and just 9.3% underweight. Slightly more participants were delivering their first child (56.6%) than their second or more. Most of the women were married (82.4%), reported no household smoking during pregnancy (81.7%) and were in their first trimester (68.5%) on 9/11. The majority of participants reported more than a high school degree (63.8%), with roughly the same proportion reporting just a high school degree (17.2%) or less than a high school degree (19.0%). Participants in the overall study population (n = 329) versus the analysis population (n = 279) were similar across most study variables; however, participants in the analysis population were slightly older (31.0 versus 30.3 years) and were more likely to be in their second/third trimester (31.5% versus 29.2%) on 9/11 compared to those participants in the overall study population (Table 2).

Comparing PFAS concentrations across sociodemographic subgroups revealed some differences (Fig. 3). Older age was associated with higher PFHxS concentrations and female newborns had higher PFOA concentrations. PFNA concentrations were higher in women exposed to the WTC disaster during their first trimester compared with women who were later on in their pregnancy on 9/11. A post hoc sensitivity analysis conducted to evaluate PFNA concentrations in the 18 women who were not yet pregnant on 9/11 revealed that PFNA concentrations were highest in this subgroup (data not shown). A higher pre-pregnancy BMI was associated with lower PFOS and PFNA concentrations. Higher education was also associated with lower PFOS and PFNA, but with higher PFHxS. Race was associated with all four PFAS concentrations. Asian race was associated with higher PFOS and PFNA, but lower PFOA concentrations. Black race was associated with lower concentrations for all four PFAS variables. White race was associated with lower PFOS and PFNA but higher PFOA and PFHxS. Home smoking exposure during pregnancy, marital status and parity were not significantly associated with any PFAS concentrations.

3.2. Associations between WTC exposure and PFAS concentrations

In fully adjusted models (Table 3), living or working within two miles of the WTC site in the four weeks following the event, was associated with 13% higher PFOA concentrations compared with those not living or working within two miles of the site (reference group) [GMR (95% CI): 1.13 (1.01, 1.27)]. Further, living within two miles of the WTC site regardless of work location, was associated with a 17% higher PFOA concentration compared with the reference group [GMR (95% CI): 1.17 (1.03, 1.33)]. Working but not living within two miles of the site was associated with a non-significant increase in PFOA concentrations [GMR (95% CI): 1.07 (0.92, 1.25)]. There were no other significant associations between WTC exposure group and PFAS concentration; however, there was a general trend of increases in the other three PFAS (PFOS, PFHxS and PFNA) concentrations for those living within two miles of the WTC site compared with those not living or working within two miles of the site. Of note, this trend was not apparent when those who worked but did not live within two miles of the WTC site were compared to the reference group.

Findings from **s**ensitivity analyses conducted in just cord blood samples (Supplemental Table 2), among participants with local fish intake data available additionally adjusted for that variable (data not shown) and using multiple imputation to fill in missing values in covariates (data not shown) were consistent with main analyses.

4. Discussion

In this study of women who delivered children in hospitals near the WTC disaster, who were pregnant during or within the weeks following the 9/11/2001 event, we observed significant increases in PFOA concentrations among participants who worked or lived within two miles of the WTC site compared with those who did not. Further, we observed stronger associations for those who lived within two miles of the site, regardless of where they worked, compared to those who worked but did not live within two miles of the site. These findings add to the minimal existing research available on trends in cord blood PFAS concentrations across sociodemographic variables in the US. In addition, our results provide evidence that exposure to the WTC disaster during pregnancy resulted in increases in cord blood PFAS concentrations, specifically PFOA. This work identifies a potentially vulnerable and overlooked population, children exposed to the WTC in utero, who should be monitored for later life effects resulting from these early life exposures.

Our study's finding of detectable PFOA and PFOS concentrations in all cord blood samples and in the majority of samples for PFNA and PFHxS, confirm previous evidence (Apelberg et al., 2007a; Midasch et al., 2007; Manzano-Salgado et al., 2015; Inoue et al., 2004; Monroy et al., 2008; Kim et al., 2011) that PFAS can cross the placental barrier, potentially harming the developing fetus. Indeed, in addition to substantial experimental evidence on the

Table 1
Geometric mean concentrations (ng/mL) and percent above detection of perfluoroalkyl substances (PFAS) in cord blood, maternal serum and cord + transformed maternal serum.

PFAS	N	LOQ	% Above LOQ	Geometric Mean (Range)[a]
PFOS				
Cord Blood	231	0.20	100%	6.27 (1.05, 33.7)
Maternal Serum	48	0.20	100%	11.9 (2.90, 30.9)
Cord Blood + Transformed Maternal Serum	279	0.20	100%	6.03 (1.05, 33.7)
PFOA				
Cord Blood	231	0.08	100%	2.37 (0.18, 8.14)
Maternal Serum	48	0.08	100%	2.42 (0.88, 5.06)
Cord Blood + Transformed Maternal Serum	279	0.08	100%	2.31 (0.18, 8.14)
PFNA				
Cord Blood	231	0.20	86%	0.45 (<LOQ, 10.3)
Maternal Serum	48	0.20	96%	0.45 (<LOQ, 1.93)
Cord Blood + Transformed Maternal Serum	279	0.20	88%	0.43 (<LOQ, 10.3)
PFHxS				
Cord Blood	231	0.08	99%	0.69 (<LOQ, 15.8)
Maternal Serum	48	0.08	100%	0.94 (0.35, 3.20)
Cord Blood + Transformed Maternal Serum	279	0.08	99%	0.67 (<LOQ, 15.8)
PFDS				
Cord Blood	231	0.08	97%	0.13 (<LOQ, 0.64)
Maternal Serum	48	0.08	98%	0.16 (<LOQ, 0.82)
PFOSA				
Cord Blood	231	0.08	0%	<LOQ
Maternal Serum	48	0.08	0%	<LOQ
PFBS				
Cord Blood	231	0.08	<1%	<LOQ (<LOQ, 0.28)
Maternal Serum	48	0.08	0%	<LOQ
PFHxA				
Cord Blood	231	0.08	15%	<LOQ (<LOQ, 10.8)
Maternal Serum	48	0.08	19%	<LOQ (<LOQ, 6.01)
PFHpA				
Cord Blood	231	0.08	36%	<LOQ (<LOQ, 0.59)
Maternal Serum	48	0.08	23%	<LOQ (<LOQ, 0.23)
PFDA				
Cord Blood	231	0.08	45%	<LOQ (<LOQ, 1.69)
Maternal Serum	48	0.08	75%	0.13 (<LOQ, 0.75)
PFUnDA				
Cord Blood	231	0.20	20%	<LOQ (<LOQ, 3.27)
Maternal Serum	48	0.20	13%	<LOQ (<LOQ, 0.87)
PFDoDA				
Cord Blood	231	0.20	7%	<LOQ (<LOQ, 0.63)
Maternal Serum	48	0.20	0%	<LOQ

Abbreviations: Limit of Quantification (LOQ); Interquartile Range (IQR); perfluorobutane sulfonate (PFBS); perfluorodecane sulphonate (PFDS); perfluorodecanoate (PFDA); perfluorododecanoic acid (PFDoDA); Perfluoroheptanoic acid (PFHpA); perfluorohexanesulfonic acid (PFHxS); Perfluorohexanoic acid (PFHxA); perfluorononanoic acid (PFNA); Perfluorooctanesulfonamide (PFOSA); perfluorooctane sulfonate (PFOS); perfluorooctanoic acid (PFOA); perfluoroundecanoic acid (PFUnDA).

[a] Geometric mean is listed as <LOQ if >50% of observations are < LOD.

developmental toxicity of PFOS (Lau et al., 2004; Negri et al., 2017), numerous epidemiological studies have reported associations between prenatal PFAS exposure and adverse health outcomes, including reductions in birth weight (Bach et al., 2015; Negri et al., 2017; Apelberg et al., 2007b), birth length (Fei et al., 2008), abdominal circumference (Fei et al., 2008), ponderal index (Apelberg et al., 2007b) and head circumference (Apelberg et al., 2007b); immune effects (Okada et al., 2012; Wang et al., 2011; Dalsager et al., 2016; Impinen et al., 2018; Granum et al., 2013; Pennings et al., 2016); and hormonal (Kim et al., 2011; Goudarzi et al., 2017; Itoh et al., 2016), behavioral (Lien et al., 2016; Quaak et al., 2016) and neurological (Liew et al., 2014; Goudarzi et al., 2016; Wang et al., 2015) outcomes.

In response to PFAS toxicity as well as their ubiquity and persistence in the environment and in humans, substantial efforts have been made to reduce their production (Technical Fact Sheet, 2017). Still, while an analysis of exposure trends using NHANES data from 1999 to 2008 showed marked reductions in PFOS over time, decreases in PFOA and PFHxS were minimal, and increases were seen for PFNA (Kato et al., 2011). Food and drinking water ingestion, followed by dust inhalation, have been identified as main pathways of exposure for PFOA and PFOS, but less is known regarding other PFAS including PFNA and PFHxS (Fromme et al., 2009). Further, patterns and determinants of exposure are incompletely understood, particularly for cord blood. The limited research and the unique sensitivity of the gestational period to chemical exposures, highlights the importance of additional studies on this topic. Our finding of higher PFOS in Asian participants compared to Black, White or other, is consistent with the only other study to evaluate trends in cord blood PFAS in the US. (Apelberg et al., 2007a) We also found higher PFNA cord blood in Asian participants compared to other races, which is a novel finding for cord blood but consistent with analyses in pregnant women (Sagiv et al., 2015). The observed higher concentrations of PFNA and PFOS in Asian participants versus other races is also consistent with national trends for these PFAS in adult serum samples (Fourth National Report on, 2018). Our results of lower PFOA and PFHxS in black versus white participants are consistent with studies evaluating trends by race in pregnant women (Kato et al., 2014; Sagiv et al., 2015) and children (Harris et al., 2017) in the US. In addition, our findings of lower PFOS and PFNA with higher BMI confirm a previous US-based study in pregnant women (Kato et al., 2014). Trends in PFAS concentrations across education subgroups varied by compound in our study: we report lower PFNA and PFOS

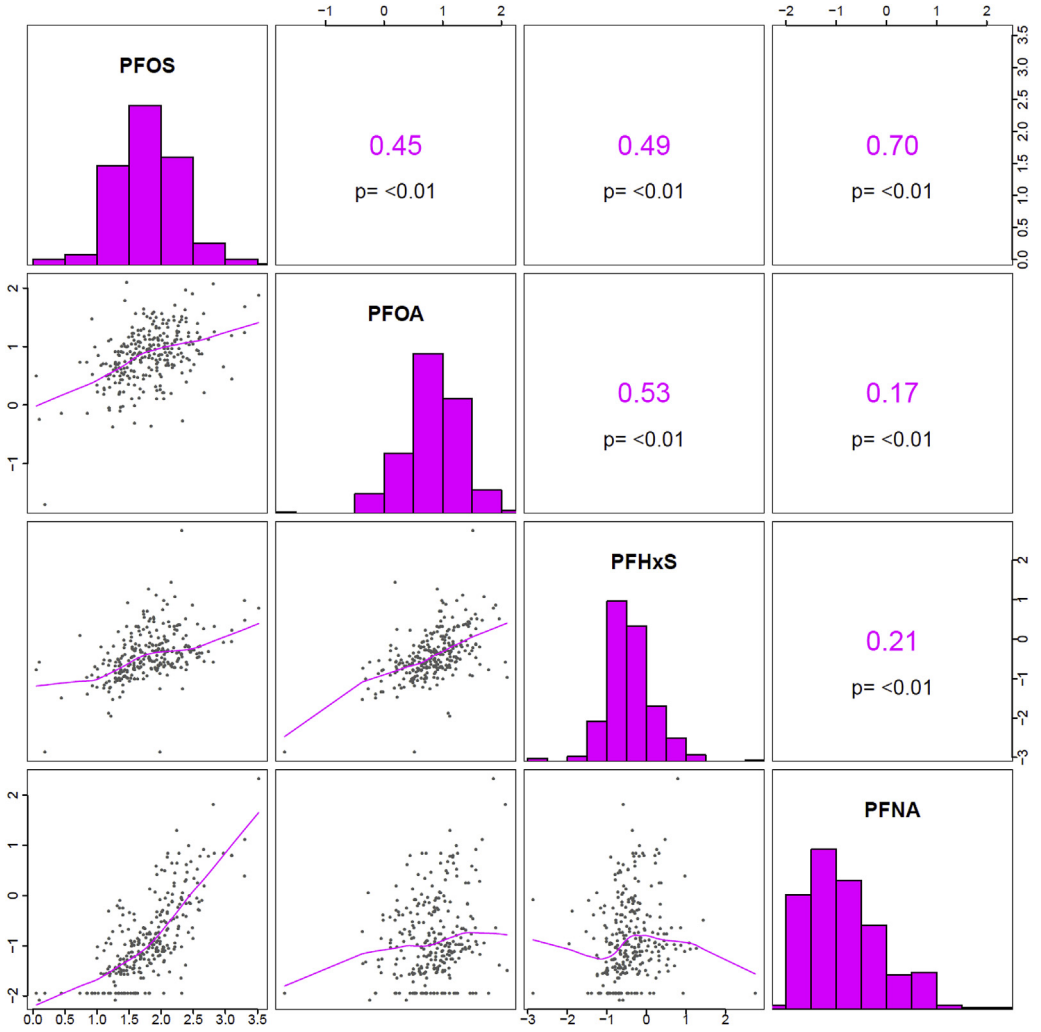

Fig. 2. Correlation Matrix of Perfluroalkyl Substances. Histograms of, and spearman correlations between, log-transformed perfluroalkyl substances. Abbreviations: perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA).

but higher PFHxS with higher education, in agreement with some (Kato et al., 2014; Sagiv et al., 2015; Harris et al., 2017; Lien et al., 2013) but not all (Harris et al., 2017) studies. In regard to WTC-related exposure, our finding of higher PFNA in women who were exposed to the WTC disaster earlier in their pregnancy may reflect the longer duration of exposure following 9/11 before delivery, compared with women who were further along in their pregnancy during the disaster. This is supported by the finding that women who were not yet pregnant on 9/11 had the highest concentrations of PFNA. Still it's unclear why this finding would be evident for PFNA and not the other PFAS. Our finding of higher PFOA in female cord blood is consistent with a previous US-based cord blood PFAS analysis (Apelberg et al., 2007a). The mechanism behind the higher levels seen in female cord blood is unclear. Further, in nationally representative analyses in adults, higher PFOA in males has been consistently reported (Kato et al., 2011; Fourth National Report on, 2018). Finally, our finding of higher PFHxS with higher maternal age is consistent with previous studies (Apelberg et al., 2007a; Kato et al., 2014; Harris et al., 2017; Manzano-Salgado et al., 2016). It is interesting to note the apparent similarities in trends across education, BMI and race between PFOS and PFNA versus PFOA and PFHxS in our population. More research is needed to determine whether these data suggest a shared source between the similar PFAS that is driving these trends.

In addition to differences in PFAS concentrations across socio-demographic variables, we observed a significant association between living or working within 2 miles of the WTC site and higher PFOA concentrations. This finding contrasts with two previous studies evaluating other chemical exposures in WTC-exposed pregnant women: WTC exposure during pregnancy was not associated with significant differences in blood mercury (Lederman et al., 2008) or polybrominated diphenyl ethers (PBDEs) (Herbstman et al., 2010). However, it is consistent with two recent studies that found elevated concentrations of PFAS (Trasande et al., 2017) and dioxin (Kahn et al., 2018) in adolescents exposed to the WTC event as children; as well as a study that found higher polycyclic aromatic hydrocarbons-DNA adducts in mothers and newborns residing within one mile of the WTC disaster (Perera et al., 2005). It is not completely clear why we observed an association with PFOA and not the other PFAS measured. Studies have suggested that PFOA crosses the placental barrier more easily than PFOS, resulting in higher transplacental transfer efficiency (Midasch et al., 2007; Fei et al., 2007; Winkens et al., 2017). In turn, higher transfer efficiency has been indicated as an explanation for

Table 2
Participant characteristics in full versus final study dataset.

Variable	Full	Final Dataset	P-value
N (%)	329 (100)[a]	279 (84.8)	
Maternal Age	30.3 (26.7–34.5)	31.0 (27.3–34.6)	0.001
Gender, n (%)			
Female	168 (51.1)	146 (52.3)	0.352
Male	161 (48.9)	133 (47.7)	
Race, n (%)			
Black	50 (16.2)	45 (16.1)	0.933
White	133 (43.2)	122 (43.7)	
Asian	113 (36.7)	101 (36.2)	
Other	12 (3.9)	11 (3.9)	
BMI, n (%)			
Underweight	31 (9.5)	26 (9.3)	0.489
Normal	231 (70.9)	201 (72.0)	
Overweight/Obese	64 (19.6)	52 (18.6)	
Parity, n (%)			
Primiparous	188 (57.3)	158 (56.6)	0.658
Multiparous	140 (42.7)	121 (43.4)	
Marital Status, n (%)			
Single	64 (19.5)	49 (17.6)	0.064
Married	265 (80.5)	230 (82.4)	
Trimester on 9/11, n (%)			
≤91 GA in days	233 (70.8)	191 (68.5)	0.04
>91 GA in days	96 (29.2)	88 (31.5)	
Education, n (%)			
< High School Degree	61 (18.5)	53 (19.0)	0.836
High School Degree	56 (17.0)	48 (17.2)	
> High School Degree	212 (64.4)	178 (63.8)	
Smoking Exposure, n (%)			
No Household Smoking	270 (82.1)	228 (81.7)	0.852
Any Household Smoking	59 (17.9)	51 (18.3)	

Abbreviations: body mass index (BMI), gestational age (GA), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA).

[a] Sample size in full dataset varies by some characteristics (PFASs variables: n = 302; Race: n = 308; BMI: n = 326; Parity: n = 328).

significant associations between PFOA and adverse health outcomes in the absence of significant findings for other PFAS (Fei et al., 2007). It is possible that a high transplacental transfer efficiency for PFOA, resulting in cord blood levels more influenced by maternal exposures, might explain the association we see between WTC exposure and cord blood PFOA versus the other PFAS evaluated in this study. We were unable to evaluate transplacental transfer efficiency for the PFAS in our population because we did not have access to paired maternal-cord samples.

PFAS was not measured in WTC dust (Landrigan et al., 2004), however, it is also possible dust and smoke from the WTC collapse and subsequent fires resulted in greater relative increases in PFOA than other PFAS due to differences in exposure sources related to the disaster across PFAS compounds. For example, PFAS are the active ingredient in aqueous film-forming foam (i.e., fire-fighting foam), which would likely have been used to help extinguish fires resulting from the WTC disaster. It's difficult to know which PFAS may have been more concentrated in the foam used during the WTC collapse due to the proprietary nature of fire-fighting foam mixtures, as well as the changes in formulations by year of production and manufacturer (Moody, 1999); however, it's possible PFOA was the dominant PFAS. This may also be true of other PFAS exposure sources specific to the WTC collapse. Dust samples from office buildings have been reported to have higher PFAS concentrations than residences and vehicles (Fraser et al., 2013); further, PFAS precursors in office air samples have been associated with PFOA serum concentrations, but not PFOS, in office workers (Fraser et al., 2012). A study evaluating serum PFAS in WTC first responders reported 2-fold higher PFOA and PFHxS concentrations, yet lower PFOS, than the general US population, suggesting higher WTC-related PFOA and PFHxS exposures compared to PFOS (Tao et al., 2008). Still, a recent study conducted in WTC-exposed children, reported significantly higher concentrations of all four PFAS compared to a matched unexposed control group (Trasande et al., 2017). Just two other studies have evaluated cord blood PFAS in US populations: cord blood PFOA in our population (median = 2.38 ng/mL) was similar (including the "exposed" population) to concentrations in both Baltimore, MD (geometric mean = 1.6 ng/mL) (Apelberg et al., 2007a) and Cincinnati, Ohio (median = 3.1 ng/mL) (Kato et al., 2014) birth cohorts. Despite comparable overall PFOA levels to other studied cities, the significant increases in PFOA concentrations observed with WTC exposure still warrant attention. Indeed, increases in PFOA at levels in the range of our cohort were associated with significant reductions in fetal growth, providing evidence that even minor increases in prenatal exposure may cause harm (Apelberg et al., 2007b).

Our findings also highlight the often overlooked importance of indoor exposures as a source of exposure in the event of both manmade and natural environmental disasters. Further, the stronger association that we found with home exposure versus just work exposure, emphasizes the significance, in particular, of home exposures to chemical body burdens in the event of an environmental disaster. This is supported by other WTC studies, which have found higher PFAS in children exposed to WTC-related home dust exposure versus dust cloud exposure (Trasande et al., 2017), as well as higher dioxin levels in children exposed to WTC house dust even after adjustment for dust cloud exposure (Kahn et al., 2018).

This study has limitations that should be considered when interpreting findings. Given the long half-life of PFAS and the single measurement of PFAS concentrations used in this study, we cannot rule out another source of exposure that could explain the observed differences reported for PFOA or could have masked differences we did not observe for the other PFAS. However, contaminated drinking water, a significant potential source of PFAS, would not be an exposure source for this population as NYC drinking water is drawn from upstate watersheds, isolated from the WTC disaster. Further, a sensitivity analysis adjusting for local fish intake (caught from the Hudson River) to account for potential confounding by this exposure source, yielded consistent results with main analyses.

5. Conclusions

Living or working within 2 miles of the WTC site was associated with increases in PFOA cord blood among women who were pregnant at the time of, or within the weeks following, the WTC disaster. These results identify a vulnerable population that should be monitored for the development of later-life health effects arising from these early life exposures; highlighting the importance of longitudinal analyses in this cohort. WTC-related home exposures, specifically, appear to be a driving factor in elevating blood levels of PFAS, and potentially other chemicals, and indicate that home exposures should be an important focus of cleanup in the event of other environmental disasters.

Funding

This work was supported by grants 1U01eOH010714-01A1, 1U01eOH010394-01A1, 1U01eOH011299-01A1 from NIOSH; the September 11th Fund of the New York Community Trust and United Way of New York City; the New York Times 9/11 Neediest Fund; the National Philanthropic Trust; and the National Institute of Environmental Health Sciences grant ES09089.

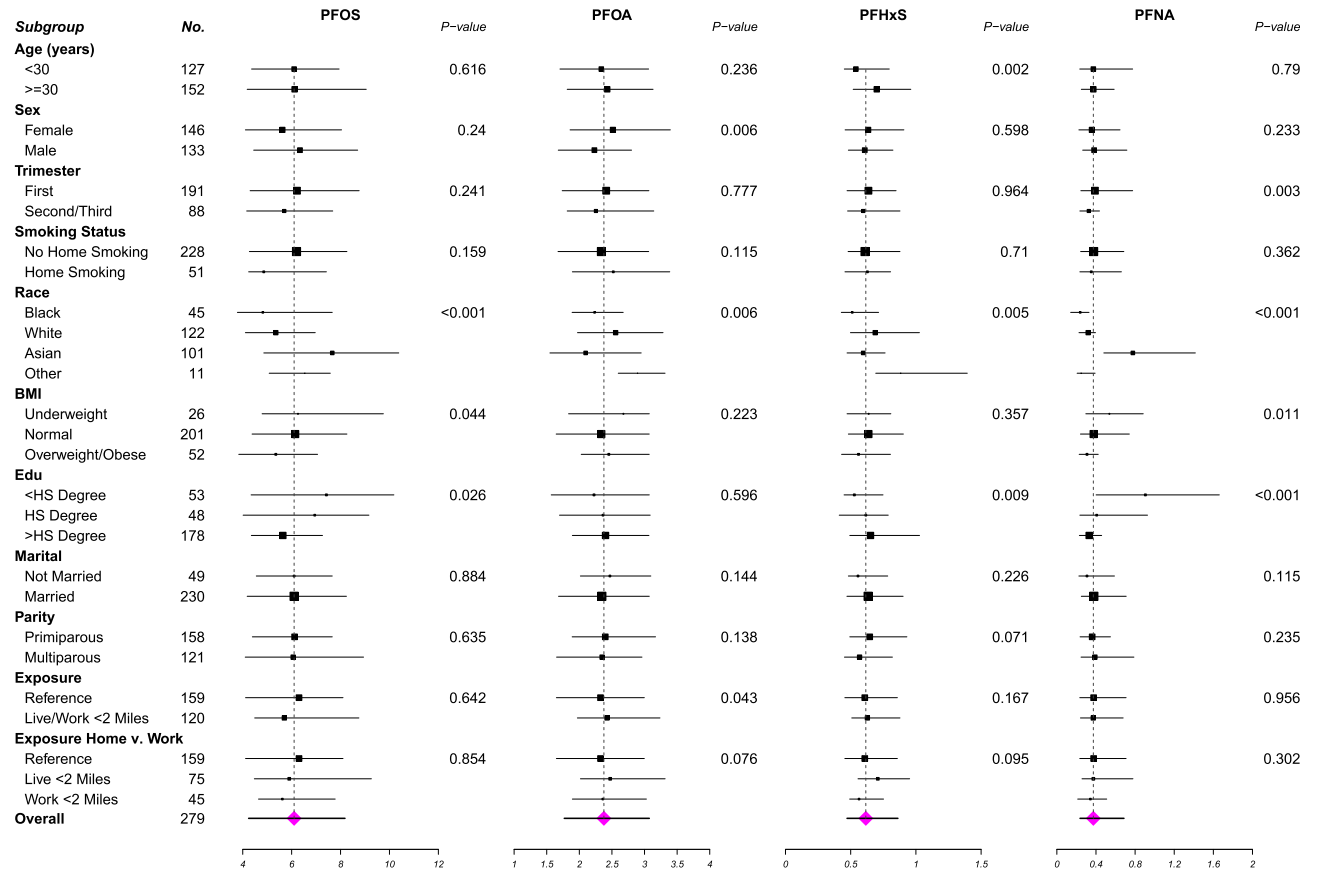

Fig. 3. Population Characteristics by Perfluroalkyl Substance Concentrations. Squares represent the median levels of metabolites and lines represent the interquartile range in each subcategory. P-values calculated from Mann-Whitney U Tests for subgroups with two categories and Kruskal-Wallis Tests for subgroups with three categories. Abbreviations: Body Mass Index (BMI), High School (HS), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA).

Table 3
Geometric mean ratios of perfluroalkyl substances world trade center exposure categories.

PFAS	Model 1	Model 2	Model 3
PFOA			
Reference (n = 159)	1	1	1
Live 2 Miles (n = 75)	1.18 (1.04, 1.35)	1.17 (1.03, 1.33)	1.17 (1.03, 1.33)
Work 2 Miles (n = 45)	1.09 (0.93, 1.27)	1.05 (0.89, 1.22)	1.07 (0.92, 1.25)
Reference (n = 159)	1	1	1
Live or Work < 2 Miles (n = 120)	1.15 (1.03, 1.28)	1.12 (1.00, 1.25)	1.13 (1.01, 1.27)
PFOS			
Reference (n = 159)	1	1	1
Live 2 Miles (n = 75)	1.06 (0.92, 1.22)	1.05 (0.92, 1.21)	1.02 (0.89, 1.18)
Work 2 Miles (n = 45)	1.00 (0.85, 1.19)	1.00 (0.85, 1.19)	1.00 (0.84, 1.18)
Reference (n = 159)	1	1	1
Live or Work < 2 Miles (n = 120)	1.04 (0.92, 1.17)	1.03 (0.92, 1.17)	1.01 (0.90, 1.14)
PFHxS			
Reference (n = 159)	1	1	1
Live 2 Miles (n = 75)	1.16 (0.98, 1.37)	1.12 (0.95, 1.33)	1.12 (0.95, 1.32)
Work 2 Miles (n = 45)	1.00 (0.82, 1.22)	0.93 (0.75, 1.14)	0.95 (0.78, 1.17)
Reference (n = 159)	1	1	1
Live or Work < 2 Miles (n = 120)	1.09 (0.95, 1.27)	1.05 (0.90, 1.21)	1.06 (0.91, 1.22)
PFNA			
Reference (n = 159)	1	1	1
Live 2 Miles (n = 75)	1.13 (0.91, 1.41)	1.13 (0.93, 1.38)	1.06 (0.89, 1.26)
Work 2 Miles (n = 45)	0.83 (0.64, 1.08)	0.93 (0.73, 1.18)	0.89 (0.72, 1.09)
Reference (n = 159)	1	1	1
Live or Work < 2 Miles (n = 120)	1.01 (0.83, 1.22)	1.05 (0.88, 1.25)	0.99 (0.85, 1.15)

Model 1: Unadjusted.
Model 2: Adjusted for Maternal Age, Child Gender, Trimester on 9/11, Maternal Pre-pregnancy BMI, Maternal Edu, Parity, Marital Status, and Household Smoking Status.
Model 3: Model 2 adjustments + Race.
Abbreviations: perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2018.12.018.

References

Apelberg, B.J., et al., 2007. Determinants of fetal exposure to polyfluoroalkyl compounds in Baltimore, Maryland. Environ. Sci. Technol. 41 (11), 3891–3897.

Apelberg, B.J., et al., 2007. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. Environ. Health Perspect. 115 (11), 1670–1676.

Bach, C.C., et al., 2015. Perfluoroalkyl and polyfluoroalkyl substances and human fetal growth: a systematic review. Crit. Rev. Toxicol. 45 (1), 53–67.

Dalsager, L., et al., 2016. Association between prenatal exposure to perfluorinated compounds and symptoms of infections at age 1-4years among 359 children in the Odense Child Cohort. Environ. Int. 96, 58–64.

Fei, C., et al., 2007. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. Environ. Health Perspect. 115 (11), 1677–1682.

Fei, C., et al., 2008. Fetal growth indicators and perfluorinated chemicals: a study in the Danish National Birth Cohort. Am. J. Epidemiol. 168 (1), 66–72.

Fourth National Report on Human Exposure to Environmental Chemicals, 2018. Centers for Disease Control and Prevention.

Fraser, A.J., et al., 2012. Polyfluorinated compounds in serum linked to indoor air in office environments. Environ. Sci. Technol. 46 (2), 1209–1215.

Fraser, A.J., et al., 2013. Polyfluorinated compounds in dust from homes, offices, and vehicles as predictors of concentrations in office workers' serum. Environ. Int. 60, 128–136.

Fromme, H., et al., 2009. Perfluorinated compounds–exposure assessment for the general population in Western countries. Int. J. Hyg Environ. Health 212 (3), 239–270.

Goudarzi, H., et al., 2016. Prenatal exposure to perfluorinated chemicals and neurodevelopment in early infancy: the Hokkaido Study. Sci. Total Environ. 541, 1002–1010.

Goudarzi, H., et al., 2017. The association of prenatal exposure to perfluorinated chemicals with glucocorticoid and androgenic hormones in cord blood samples: the Hokkaido study. Environ. Health Perspect. 125 (1), 111–118.

Granum, B., et al., 2013. Pre-natal exposure to perfluoroalkyl substances may be associated with altered vaccine antibody levels and immune-related health outcomes in early childhood. J. Immunot. 10 (4), 373–379.

Harris, M.H., et al., 2017. Predictors of per- and polyfluoroalkyl substance (PFAS) plasma concentrations in 6-10 Year old American children. Environ. Sci. Technol. 51 (9), 5193–5204.

Herbstman, J.B., et al., 2010. Prenatal exposure to PBDEs and neurodevelopment. Environ. Health Perspect. 118 (5), 712–719.

Impinen, A., et al., 2018. Prenatal exposure to perfluoralkyl substances (PFASs) associated with respiratory tract infections but not allergy- and asthma-related health outcomes in childhood. Environ. Res. 160, 518–523.

Inoue, K., et al., 2004. Perfluorooctane sulfonate (PFOS) and related perfluorinated compounds in human maternal and cord blood samples: assessment of PFOS exposure in a susceptible population during pregnancy. Environ. Health Perspect. 112 (11), 1204–1207.

Itoh, S., et al., 2016. Association of perfluoroalkyl substances exposure in utero with reproductive hormone levels in cord blood in the Hokkaido Study on Environment and Children's Health. Environ. Int. 94, 51–59.

Kahn, L.G., et al., 2018. Adolescents exposed to the World Trade Center collapse have elevated serum dioxin and furan concentrations more than 12years later. Environ. Int. 111, 268–278.

Kannan, K., et al., 2004. Perfluorooctanesulfonate and related fluorochemicals in human blood from several countries. Environ. Sci. Technol. 38 (17), 4489–4495.

Kataria, A., et al., 2015. Association between perfluoroalkyl acids and kidney function in a cross-sectional study of adolescents. Environ. Health 14, 89.

Kato, K., et al., 2011. Trends in exposure to polyfluoroalkyl chemicals in the U.S. Population: 1999-2008. Environ. Sci. Technol. 45 (19), 8037–8045.

Kato, K., et al., 2014. Changes in serum concentrations of maternal poly- and perfluoroalkyl substances over the course of pregnancy and predictors of exposure in a multiethnic cohort of Cincinnati, Ohio pregnant women during 2003-2006. Environ. Sci. Technol. 48 (16), 9600–9608.

Kim, S., et al., 2011. Trans-placental transfer of thirteen perfluorinated compounds and relations with fetal thyroid hormones. Environ. Sci. Technol. 45 (17), 7465–7472.

Landrigan, P.J., et al., 2004. Health and environmental consequences of the world trade center disaster. Environ. Health Perspect. 112 (6), 731–739.

Lau, C., Butenhoff, J.L., Rogers, J.M., 2004. The developmental toxicity of perfluoroalkyl acids and their derivatives. Toxicol. Appl. Pharmacol. 198 (2), 231–241.

Lederman, S.A., et al., 2004. The effects of the World Trade Center event on birth outcomes among term deliveries at three lower Manhattan hospitals. Environ. Health Perspect. 112 (17), 1772–1778.

Lederman, S.A., et al., 2008. Relation between cord blood mercury levels and early child development in a World Trade Center cohort. Environ. Health Perspect. 116 (8), 1085–1091.

Lien, G.W., et al., 2013. Neonatal-maternal factors and perfluoroalkyl substances in cord blood. Chemosphere 92 (7), 843–850.

Lien, G.W., et al., 2016. Perfluoroalkyl substances in cord blood and attention deficit/hyperactivity disorder symptoms in seven-year-old children. Chemosphere 156, 118–127.

Liew, Z., et al., 2014. Prenatal exposure to perfluoroalkyl substances and the risk of congenital cerebral palsy in children. Am. J. Epidemiol. 180 (6), 574–581.

Manzano-Salgado, C.B., et al., 2015. Transfer of perfluoroalkyl substances from mother to fetus in a Spanish birth cohort. Environ. Res. 142, 471–478.

Manzano-Salgado, C.B., et al., 2016. Variability of perfluoroalkyl substance concentrations in pregnant women by socio-demographic and dietary factors in a Spanish birth cohort. Environ. Int. 92–93, 357–365.

Midasch, O., et al., 2007. Transplacental exposure of neonates to perfluorooctanesulfonate and perfluorooctanoate: a pilot study. Int. Arch. Occup. Environ. Health 80 (7), 643–648.

Monroy, R., et al., 2008. Serum levels of perfluoroalkyl compounds in human maternal and umbilical cord blood samples. Environ. Res. 108 (1), 56–62.

Moody, C.F.,J.A., 1999. Determination of perfluorocarboxylates in groundwater impacted by fire-fighting activity. Environ. Sci. Technol. 33 (16), 2800–2806.

Negri, E., et al., 2017. Exposure to PFOA and PFOS and fetal growth: a critical merging of toxicological and epidemiological data. Crit. Rev. Toxicol. 47 (6), 482–508.

Okada, E., et al., 2012. Prenatal exposure to perfluorinated chemicals and relationship with allergies and infectious diseases in infants. Environ. Res. 112, 118–125.

Olsen, G.W., Butenhoff, J.L., Zobel, L.R., 2009. Perfluoroalkyl chemicals and human fetal development: an epidemiologic review with clinical and toxicological perspectives. Reprod. Toxicol. 27 (3–4), 212–230.

Pennings, J.L., et al., 2016. Cord blood gene expression supports that prenatal exposure to perfluoroalkyl substances causes depressed immune functionality in early childhood. J. Immunot. 13 (2), 173–180.

Perera, F.P., et al., 2005. Relationships among polycyclic aromatic hydrocarbon-DNA adducts, proximity to the World Trade Center, and effects on fetal growth. Environ. Health Perspect. 113 (8), 1062–1067.

Quaak, I., et al., 2016. Prenatal exposure to perfluoroalkyl substances and behavioral development in children. Int. J. Environ. Res. Publ. Health 13 (5).

Sagiv, S.K., et al., 2015. Sociodemographic and perinatal predictors of early pregnancy per- and polyfluoroalkyl substance (PFAS) concentrations. Environ. Sci. Technol. 49 (19), 11849–11858.

Sakr, C.J., et al., 2007. Cross-sectional study of lipids and liver enzymes related to a serum biomarker of exposure (ammonium perfluorooctanoate or APFO) as part of a general health survey in a cohort of occupationally exposed workers. J. Occup. Environ. Med. 49 (10), 1086–1096.

Taniyasu, S., et al., 2005. Analysis of fluorotelomer alcohols, fluorotelomer acids, and short- and long-chain perfluorinated acids in water and biota. J. Chromatogr. A 1093 (1–2), 89–97.

Tao, L., et al., 2008. Biomonitoring of perfluorochemicals in plasma of New York State personnel responding to the World Trade Center disaster. Environ. Sci. Technol. 42 (9), 3472–3478.

Technical Fact Sheet, 2017. Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA). U.S.E.P. Agency.

Trasande, L., et al., 2017. Serum perfluoroalkyl substances in children exposed to the world trade center disaster. Environ. Res. 154, 212–221.

Wang, I.J., et al., 2011. The effect of prenatal perfluorinated chemicals exposures on pediatric atopy. Environ. Res. 111 (6), 785–791.

Wang, Y., et al., 2015. Prenatal exposure to perfluroalkyl substances and children's IQ: the Taiwan maternal and infant cohort study. Int. J. Hyg Environ. Health 218 (7), 639–644.

Water, O.o. (Ed.), 2016. Health Effects Support Document for Perfluorooctanoic Acid (PFOA) (Washington, DC).

Water, O.o. (Ed.), 2016. Health Effects Support Document for Perfluorooctane Sulfonate (PFOS) (Washington, DC).

Winkens, K.,V.R., Berger, U., Cousins, I., 2017. Early life exposure to per- and polyfluoroalkyl substances (PFASs): a critical review. Emerging Contaminants 3 (2), 55–68.

Your 9/11 health Care. NYC 9/11 Health [cited 2018; Available from: https://www1.nyc.gov/site/911health/enrollees/9-11-treatment-referral-program.page.