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Prenatal Exposure to Perfluorooctanoate and Risk of Overweight at 20 Years of Age: A Prospective Cohort Study

Thorhallur I. Halldorsson,1,2,3 Dorte Ryttner,4 Line Småstuen Haug,5 Bodil Hammer Bech,4 Inge Danielsen,1 Georg Becher,5,6 Tine Brink Henriksen,7 and Sjurdur F. Olsen1,8

1Center for Fetal Programming, Department of Epidemiology Research, Statens Serum Institute, Copenhagen, Denmark; 2Faculty of Food Science and Nutrition, University of Iceland, Reykjavik, Iceland; 3Unit for Nutrition Research, Landspitali University Hospital, Reykjavik, Iceland; 4Department of Public Health, Section for Epidemiology, Aarhus University, Denmark; 5Division of Environmental Medicine, Norwegian Institute of Public Health, Oslo, Norway; 6Department of Analytical Chemistry, University of Oslo, Oslo, Norway; 7Department of Paediatrics, Aarhus University Hospital, Skejby, Denmark; 8Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, USA

BACKGROUND: Perfluoroalkyl acids are persistent compounds used in various industrial applications. Of these compounds, perfluorooctanoate (PFOA) is currently detected in humans worldwide. A recent study on low-dose developmental exposure to PFOA in mice reported increased weight and elevated biomarkers of adiposity in postpubertal female offspring.

METHODS: A prospective cohort of 665 Danish pregnant women was recruited in 1988–1989 with offspring follow-up at 20 years. PFOA was measured in serum from gestational week 30. Offspring body mass index (BMI) and waist circumference were recorded at follow-up (n = 665), and biomarkers of adiposity were quantified in a subset (n = 422) of participants.

RESULTS: After adjusting for covariates, including maternal prepregnancy BMI, smoking, education, and birth weight, in utero exposure to PFOA was positively associated with anthropometry at 20 years in female but not male offspring. Adjusted relative risks comparing the highest with lowest quartile (median: 5.8 vs. 2.3 ng/mL) of maternal PFOA concentration were 3.1 (95% confidence interval: 1.4, 6.9) for overweight or obese (BMI ≥ 25 kg/m²) and 3.0 (95% CI: 1.3, 6.8) for waist circumference > 88 cm among female offspring. This corresponded to estimated increases of 1.6 kg/m² (95% CI: 0.6, 2.6) and 4.3 cm (95% CI: 1.4, 7.3) in average BMI and waist circumference, respectively. In addition, maternal PFOA concentrations were positively associated with serum insulin and leptin levels and inversely associated with adiponectin levels in female offspring. Similar associations were observed for males, although point estimates were less precise because of fewer observations. Maternal perfluorooctane sulfonate (PFOS), perfluorooctane sulfonamide (PFOSA), and perfluorononanoate (PFNA) concentrations were not independently associated with offspring anthropometry at 20 years.

CONCLUSIONS: Our findings on the effects of low-dose developmental exposures to PFOA are in line with experimental results suggesting obesogenic effects in female offspring at 20 years of age.

KEY WORDS: offspring obesity, overweight, perfluoroalkyl compounds, PFOA, pregnancy, prenatal exposure. Environ Health Perspect 120:668–673 (2012). http://dx.doi.org/10.1289/ehp.1104034 [Online 3 February 2012]

Because of their repellent properties and low surface tension, fluorocarbons have been used extensively for more than half a century in various commercial applications, including carpets, textiles, personal care products, leveling and wetting agents and in food-contact materials. D’eon and Mabury 2011). Use and production of fluorinated chemicals has resulted in the environmental presence of perfluoroalkyl compounds (PFCAs) and perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) in blood (D’eon et al. 2011). PFAAs accumulate primarily via binding to albumin in blood (Becker et al. 2010; Jones et al. 2003), and they are readily transported across the placenta (Monroy et al. 2008). PFAAs are found in highest concentrations in the liver (Hundley et al. 2006; Maestri et al. 2006) and low-dose human exposures to PFOA and PFOS have been associated with modest increases in liver enzymes (Lin et al. 2010) and blood lipids (Nelson et al. 2010) in cross-sectional settings. Thus, the relevance of these findings is uncertain, however, because prospective studies have not been conducted. Findings from animal studies suggest that PFAAs may act as endocrine disruptors, affecting circulating estrogens levels through pathways such as aromatase induction in the liver (Liu et al. 1996) or through altering estrogens–progesterone ratios (Majumdar et al. 2009), although findings with respect to interactions with estrogen receptors have not been consistent (Benninghoff et al. 2011). The aim of this study was to explore these findings in environmentally exposed pregnant women with prospective offspring follow-up at 20 years of age.

Methods

The birth cohort. Between April 1988 and January 1989, 965 women with singleton pregnancies were recruited for a birth cohort study in Aarhus, Denmark (Olsen et al. 1995). This was 80% of a consecutive sample of 1,212 women attending a midwife center in Aarhus.

Address correspondence to T.I. Halldorsson, Center for Fetal Programming, Department of Epidemiology Research, Statens Serum Institut, Osterbys Boulevard 5, Building 206, 2300 Copenhagen, Denmark. Telephone: 453268800. Fax: 4532683165. E-mail: lur@ssi.dk

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the city, covering a well-defined geographical area. A face-to-face interview was conducted at a routine midwife visit in gestational week 30, covering medical history, anthropometry, diet, lifestyle, and socioeconomic factors. A blood sample was also collected, and it was immediately separated into serum, plasma, and erythrocytes and frozen at –20°C. Further information on maternal health and birth outcomes were extracted from hospital records and the Danish Medical Birth Registry.

Offspring follow-up. In 2008–2009, study mothers and offspring were contacted, and offspring were asked to fill out a Web-based questionnaire concerning their current health, lifestyle, and dietary habits and their current height and weight. In addition, a tape measure was mailed to all potential participants with instructions on how to measure their waist circumference. Offspring were also invited to participate in a 75–100-min clinical examination, which included standardized anthropometric measures and collection of a fasting blood sample that was immediately centrifuged and frozen at –80°C. The study was approved by the Danish Data Protection Agency and the Danish Council of Ethics (reference no. 20070157), and all participants gave written consent prior to inclusion into the study.

Mother–offspring pairs available for analysis. A total of 915 offspring of the 965 women with singleton pregnancies recruited in 1988–1999 were located and contacted in 2008–2009, and 692 of the offspring agreed to participate in the follow-up study. Missing values on offspring anthropometry (n = 4) and maternal blood samples (n = 23) left 665 mother–offspring pairs, or 69% of the original cohort, available for analyses. Of the 665 offspring included in this study, 423 (44% of the original cohort) attended the clinical examination, and 242 completed the Web-based questionnaire only.

Maternal PFAA samples. Serum samples from gestational week 30 were measured at the Department of Analytical Chemistry at the Norwegian Institute of Public Health in Oslo. The analytical procedure and sources of chemicals used have been described in detail elsewhere (Haug et al. 2009a). Nineteen PFAAs were analyzed, and 12 were above the limit of quantification (LOQ: 0.05 ng/mL for all PFAAs reported in this study) in one or more samples. For quantification of PFOS, the total area of the linear and branched isomers was integrated. The quality of the analytical procedure was monitored by analyzing in-house quality control samples and human serum samples from interlaboratory comparison exercises (Institut national de santé publique Québec 2009). For the interlaboratory comparison exercises, the coefficient of variation for PFOA was between 3% and 9%, depending on the concentration of the reference sample. No traces of PFAAs above LOQ were observed in any of the procedural blanks.

Offspring biomarkers of adiposity. In short, adiponectin was quantified by a time-resolved immunofluorometric assay based on two antibodies and recombinant human adiponectin (R&D Systems, Abingdon, United Kingdom), as previously described (Frystyk et al. 2005). Leptin was determined by a time-resolved immunofluorometric assay based on commercial reagents (R&D Systems) using recombinant human leptin as the standard; otherwise, quantification was carried out essentially as for adiponectin (Frystyk et al. 2005). Plasma insulin concentrations were determined by the commercial Insulin ELISA kit (Dako, Copenhagen, Denmark).

Outcome measures. Body mass index (BMI) and waist circumference measures from the clinical examination were used when available (n = 423). Self-reported measures from the Web-based questionnaire were used for the remaining 242 subjects. Although subjects tend to underestimate their height by self-report (Tokmakidis et al. 2007), relative ranks appeared to be retained, as the correlation between measured and self-reported BMI was 0.91 for both sexes (Spearman r, n = 423). Use of self-reported measures does, however, result in underestimation of cases when dichotomizing subjects as overweight and obese (BMI ≥ 25 kg/m²). In our data the sensitivity coefficient and specificity coefficients were 0.46 and 0.99, respectively, for identifying overweight and obese female offspring based on self-report. The corresponding numbers were 0.63 and 0.98 for male offspring, respectively.

Statistical analyses. The mean and SD were used to describe normal variables, whereas median and interquartile range (IQR) were used for skewed variables. Student t-tests or chi-square tests were used to test departures from the null hypothesis for normal outcomes, and the Kruskal–Wallis test was used for skewed outcomes. Linear regression was used for continuous outcomes. For dichotomous outcomes, relative risk (RR) was estimated using log-Poisson regression with robust variance estimation, as implemented in PROC GENMODE in SAS (version 9.2; SAS Institute Inc., Cary, NC, USA). All analyses were performed for males and females separately. When examining association with anthropometric outcomes, maternal PFOA concentrations were divided into quartiles and a test for linear trend was performed by using the ordinal values. For the biomarker analysis, PFOA was entered as a continuous variable.

When estimating the association between in utero PFOA concentration and offspring anthropometry at 20 years of age, we adjusted for the following potential confounders identified a priori: maternal age (continuous, no missing); maternal education (elementary schooling, high school or technical schooling, university education, higher academic education, other education, 6% missing); maternal smoking (never, < 10 and ≥ 10 cigarettes/day, 6% missing); prepregnancy BMI [restricted cubic spline regression (Durrleman and Simon 1989), 2% missing]; parity (0, 1, ≥ 2, no missing); infant birth weight (continuous, 0.2% missing); and offspring age at follow-up (continuous, 1% missing). A total of 67 subjects (10%) had missing values for one or more of the covariates included. Maternal age and parity were included because they are known predictors of PFAA exposure (Fei et al. 2007). Maternal education and smoking were included to account for potential social and lifestyle confounding. Prepregnancy BMI and birth weight were included because they are known predictors of offspring BMI (Reynolds et al. 2010). Missing covariate values were substituted using multiple imputation, as implemented in PROC MI in SAS (SAS Institute, Inc.). Because of skewed distributions, offspring biomarkers of adiposity were log-transformed when examining their association with maternal PFOA concentrations, and estimates were adjusted for offspring age and timing of blood sample collection.

Results

Nonsignificant differences in maternal PFOA concentration, prepregnancy BMI, and parity were observed between mothers whose offspring did not participate in follow-up, mothers whose offspring completed the Web-based questionnaire only, and mothers whose offspring participated in the clinical examination (Table 1). However, mothers whose offspring did not participate in follow-up were more likely to smoke during pregnancy. Females who participated in clinical examination had significantly lower BMI (= 0.8 kg/m²) compared with those who completed the Web-based questionnaire only, whereas nonsignificant differences were observed for waist circumference and current smoking. Male offspring who participated in the clinical examination were not significantly different from those who completed the Web-based questionnaire only with regard to BMI, waist circumference, and current smoking.

The median maternal PFOA serum concentration was 3.7 ng/mL (range: 0.1–19.8). Maternal PFOS, perfluorooctane sulfonamide (PFOSA), and perfluorononanoate (PFNDA) concentrations increased across quartiles of PFOA concentration (Table 2). Eight other PFAAs were quantified but were not included in analyses because concentrations were low (median: ≤ 0.4 ng/mL) and were within a narrow range (IQR < 0.2 ng/mL). Mothers in the highest quartile of PFOA concentration
were less likely to be parous (32% vs. 58%) and were younger (28.7 vs. 29.8 years) than mothers in the lowest quartile of PFOA when enrolled into the original study.

The prevalence of overweight or obesity (BMI ≥ 25 kg/m²) was similar between male and female offspring (19% and 18%, respectively), but waist circumference above action level II (Lean et al. 1995) was less common in males (3.5% > 102 cm) than in females (16.2% > 88 cm) (Table 3). All males and 70% of females with waist circumference above action level II were overweight or obese. Females were more likely than males to report that they were currently on a diet (17% vs. 6%).

Maternal PFOA concentrations were positively associated (p for trend < 0.05) with BMI and waist circumference among female offspring at 20 years of age (n = 345) in both unadjusted and covariate-adjusted analyses (Table 4). In adjusted analyses, female offspring whose mothers were in the highest quartile of PFOA concentration had 1.6 kg/m² [95% confidence interval (CI): 0.6, 2.6] higher BMI and 4.3 cm (95% CI: 1.4, 7.3) higher waist circumference compared with offspring whose mothers were in the lowest quartile. No statistically significant associations were observed for males (p for trend > 0.05, n = 320). Female offspring of mothers in the highest versus lowest PFOA quartile were also more likely to be overweight [RR = 3.1 (95% CI: 1.4, 6.9)] and to have a waist circumference above action level II at 20 years of age [3.0 (95% CI: 1.3, 6.8)] (Table 5). PFOA was not associated with overweight in male offspring, and RR estimates were consistently null. Only 11 of 320 male offspring had a waist circumference above action level II; consequently, RR estimates were unstable with wide CIs.

Among female participants who provided a blood sample at clinical examination (n = 252), maternal PFOA concentration was positively associated with insulin, leptin, and the leptin-adiponectin ratio in a gender-specific manner. The associations corresponded to a 2–7% change in these biomarkers per 1-unit increase in PFOA. Point estimates were similar for male offspring but nonsignificant (n = 170). Although the precision of the estimated associations between maternal PFOA and the biomarkers was reduced because of the small sample size for this analysis (particularly in males), associations between maternal PFOA and offspring anthropometry were comparable with those for the follow-up participants as a whole, supporting the validity of these estimates. For example, estimated increases in BMI comparing highest with lowest quartile of maternal PFOA concentration were 1.8 kg/m² (95% CI: 0.6, 3.0) and 0.6 kg/m² (95% CI: –0.7, 1.9) for female and male offspring who provided a blood sample at clinical examination, compared with 1.6 kg/m² (95% CI: 0.6, 2.6) and 0.6 kg/m² (95% CI: –0.3, 1.5) for all female and male participants, respectively.

Concerning other PFASs, we observed that PFOS, PFNA, and PFOSA (continuous variables) were in univariate analysis either borderline (p for trend = 0.05 for PFOSA) or significantly (p for trend < 0.05 for PFNA,
PFOS) positively associated with female off-
spring BMI at 20 years. However, after adjust-
ing for PFOSA, the regression coefficients be-
came nonsignificant (p for trend ≥ 0.56 in all cases, data not shown). We also found no evi-
dence that the association between maternal
PFOA concentration in offspring adiposity was
influenced by the presence of the other
PFAs quantified. For example, the
estimated increase in female offspring
BMI with a 1-ng/mL increase in maternal
PFOA in a univariate analysis was 0.43 kg/m²
(95% CI: 0.25, 0.60) compared with 0.46 kg/m²
(95% CI: 0.21, 0.71) based on a model that
included maternal PFOS, PFOSA, and PFNA
as continuous terms.

Associations with offspring BMI were also
stable with respect to maternal parity. For
female offspring of nulliparous mothers
(n = 191), we estimated a 0.46-kg/m² (95% CI:
0.27, 0.66) increase in BMI per 1-ng/mL
increase in PFOA, compared with 0.36 kg/m²
(95% CI: 0.03, 0.69) for female offspring
of parous mothers (interaction p-value 0.65).

**Discussion**

In this cohort of environmentally exposed
pregnant women, we observed a positive asso-
ciation between in utero exposure to PFOA
and the prevalence of overweight and a high
waist circumference among female offspring,
but not male offspring, at 20 years of age.
In addition, in utero exposure to PFOA was
associated with biomarkers of adiposity among
male and female offspring, although estimates
for males were not significant.

Animal studies have shown that early-life
exposures to xenoestrogens such as diethylstil-
bestrol (Newbold et al. 2008) and bisphenol-A
(Somm et al. 2009) can lead to permanent dis-
orders, such as blood lipids (Nelson et al. 2010)
and biomarkers of adiposity among
postpubertal female offspring after low-dose
(0.01–0.3 mg/kg body weight) in utero
exposure to PFOA (Hines et al. 2009). In that
study, increases in weight were most
pronounced in mid-life and were accompa-
nied by elevated levels of leptin and insu-
lin in the exposed animals. At higher doses
(≥ 1 mg/kg), weight gain was not observed.
Furthermore, exposing the offspring after
weaning as opposed to in utero also had no
effect on weight gain. In at least two animal
studies, researchers did not observe increased
body weight after in utero exposure to PFOA
(Butenhoff et al. 2004; Macon et al. 2011).

**Table 4.** Associations between in utero exposure to PFOA and the BMI at 20 years of age for females (n = 345) and males (n = 320).

<table>
<thead>
<tr>
<th>PFOA in quartiles</th>
<th>ΔBMI [mean (95% CI)]</th>
<th>ΔWaist circumference [mean (95% CI)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude</td>
<td>Adjusted†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.0 (1.9–2.1)</td>
<td>Referent</td>
</tr>
<tr>
<td>2</td>
<td>3.2 (2.9–3.7)</td>
<td>0.2 (–0.7, 1.2)</td>
</tr>
<tr>
<td>3</td>
<td>4.2 (3.7–4.8)</td>
<td>0.8 (–0.2, 1.8)</td>
</tr>
<tr>
<td>4</td>
<td>5.8 (4.8–19.8)</td>
<td>1.6 (0.6, 2.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.4 (1.2–2.8)</td>
<td>Referent</td>
</tr>
<tr>
<td>2</td>
<td>3.3 (2.8–3.7)</td>
<td>0.5 (–0.4, 1.4)</td>
</tr>
<tr>
<td>3</td>
<td>4.2 (3.7–4.8)</td>
<td>0.3 (–0.7, 1.2)</td>
</tr>
<tr>
<td>4</td>
<td>5.8 (4.8–16.6)</td>
<td>0.4 (–0.5, 1.3)</td>
</tr>
</tbody>
</table>

**Linear regression with outcome variables (BMI or waist circumference) and PFOA divided into quartiles.**

**Table 5.** Associations between in utero exposure to PFOA and risk of being overweight or having waist circumference above 100th percentile at 20 years of age for females (n = 345) and males (n = 320).

<table>
<thead>
<tr>
<th>PFOA in quartiles</th>
<th>Overweight (BMI &gt; 25 kg/m²)</th>
<th>Risk [RR (95% CI)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases/no.</td>
<td>Crude</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td>2.3 (2.8–3.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12/87</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13/87</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.4 (3.7–4.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20/90</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11/61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.2 (4.8–16.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24/86</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Males‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.3 (1.2–2.8)</td>
<td>1.00</td>
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<td>2</td>
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<td>3</td>
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<td>1.0 (0.5, 2.0)</td>
</tr>
<tr>
<td>4</td>
<td>5.8 (4.8–16.6)</td>
<td>1.0 (0.5, 2.0)</td>
</tr>
</tbody>
</table>

**Log-Poisson regression with robust variance estimation, as implemented in PROC GENMOD in SAS.**

**Table 6.** Association between in utero exposure to PFOA and offspring serum biomarkers of adiposity at 20 years of age.

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Percent changeabc</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females (n = 252)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>4.5</td>
<td>1.8, 7.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Leptin</td>
<td>4.8</td>
<td>0.5, 9.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>–2.3</td>
<td>–4.5, –0.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Leptin/adiponectin ratio</td>
<td>7.2</td>
<td>2.2, 12.5</td>
<td>0.004</td>
</tr>
</tbody>
</table>

| Males (n = 170) |                   |        |          |
| Leptin        | 4.5               | –2.6, 12.1 | 0.21    |
| Adiponectin   | –4.2              | –4.6, 12.2 | 0.25   |

The associations are limited to the subgroup of participants (n = 422) that provided blood samples at clinical examination.

**Linear regression using log-transformation for the dependent variable (continuous). The results are adjusted for time of blood sample collection (e.g., 08:00–12:30) and offspring age at follow-up.**

**Biomarker Percent change**

**Leptin/adiponectin ratio 7.2 (95% CI: 0.21, 0.71) based on a model that included maternal PFOA, PFOSA, and PFNA as continuous terms.**

**Discussion**

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studies, researchers did not observe increased
body weight after in utero exposure to PFOA
(Butenhoff et al. 2004; Macon et al. 2011).
but one study used higher doses (≥ 1 mg/kg) (Butenholz et al. 2004) and the other followed animals only until 12 weeks of age (Macon et al. 2011).

Similar to the findings of Hines et al. (2009), we observed significant associations between maternal PFOA and insulin and leptin in addition to adiponectin levels among female offspring. Changes in these biomarkers were modest, however, and corresponded to what could be expected from the observed increase in offspring BMI. The results from our biomarker analysis provide valuable insight, as elevated insulin levels predict central fat in both normal weight and overweight women (Carey et al. 1996). Therefore, these results provide added weight to our findings, as BMI and waist circumference are relatively crude measures of body composition.

The absence of an association between in utero PFOA exposure and weight gain among male offspring is noteworthy but not unexpected. Sex-specific differences with respect to weight gain have been observed for xenobiotics, where female offspring appear to be more affected (Newbold et al. 2008; Somm et al. 2009). Results for male offspring were not reported in the CD-1 mouse study (Hines et al. 2009), and experimental studies have suggested that reproductive development, but not weight gain, may be a more sensitive end point for males with respect to developmental exposures to PFAAs (Shi et al. 2007).

Despite these observations, results for male offspring in our study should be interpreted cautiously, as many study participants were still in their late adolescence, and relatively few males had high waist circumference compared with females. Because girls gain more fat mass and boys gain more fat-free mass during adolescence (Ahmed et al. 1999), weight gain in male offspring at a later age when accumulation of fat mass increases cannot be excluded.

Concerning mechanism, there are at least three potential pathways by which in utero exposure to PFOA might affect offspring weight. First, PFOA may interfere with ovary development in utero, leading to impaired estrogen synthesis among female offspring. This mechanism is supported by the observation that in utero PFOA exposure did not affect weight gain in the previously mentioned study on CD-1 mice when ovariectomy was performed in exposed offspring after delivery (Hines et al. 2009). Second, PFAAs may interact with the peroxisome proliferator-activated receptors (PPAR) PPARα and PPARγ, which are involved in lipid metabolism in adipocytes (Hines et al. 2009). Whether such an interaction can lead to sex-specific differences in weight gain remains unclear. Third, thyroid hormones might play some role: The results of one cross-sectional study suggested that PFOA exposure may lead to an increased risk of thyroid disease (Melzer et al. 2010), which is more common in females than males. A recent study from the CB Health project also observed a modest positive association of PFOA with serum thyroxine and an inverse association with T3 uptake (Knox et al. 2011). The overall evidence linking PFAAs to thyroid function is still weak (Steenland et al. 2010), particularly as prospective studies have not been conducted, and no clear effect on thyroid function has been observed in occupationally exposed individuals (Olsen and Zobel 2007).

A unique strength of our study is the long-term prospective follow-up with outcome assessment at an age where weight changes due to linear growth have leveled off, and it was possible to adjust for several prenatal factors including maternal BMI, smoking, and education. We were also able to support our findings on offspring anthropometry with assessment on serum biomarkers of adiposity in a subset of study participants. Furthermore, quantification of a total of 12 PFAAs made it possible to conclude that PFAAs other than PFOA were unlikely to play an important role in our study population, either because of a low concentration or a lack of association after adjusting for PFOA.

Concerning limitations, we acknowledge that uncertainties regarding routes of human exposure to PFAAs may have resulted in a failure to identify important confounders. We also acknowledge that maternal PFOA concentrations in late gestation may be influenced by factors such as blood volume expansion, decreased albumin concentration, and fetal uptake (Fei et al. 2007; Frederiksen 2001), and these factors may predict fetal outcomes such as birth weight (Savitz 2007). However, with a temporal separation of 20 years, our findings should be less prone to such influence. Furthermore, PFOA concentrations in samples collected at around gestational weeks 6–12 and 24 (Olsen et al. 2001) and in cord blood have been observed to be highly correlated (r = 0.8–0.9) (Fei et al. 2007).

Finally, as with all longitudinal studies, losses during follow-up are inevitable, and this is perhaps the main limitation of our study. Having quantified maternal PFOA concentrations in 874 (or 72%) of 1,212 women who were originally invited to participate, it is reassuring that exposure levels were nondifferential with respect to level of participation in the follow-up study. A higher prevalence of smoking among mothers whose offspring did not participate suggests that losses due to follow-up were related to some extent to maternal lifestyle. There were relatively modest differences in anthropometry among offspring who participated in the clinical examination and those who completed the Web-based questionnaire only. Nonetheless, our secondary analyses of offspring biomarkers of adiposity may be compromised because of the low participation rate, particularly among males.

Conclusion

In a cohort of environmentally exposed pregnant women, a positive association between in utero exposure to PFOA and the prevalence of overweight and high waist circumference was observed in female offspring at 20 years of age. Our findings are in line with recent experimental findings (Hines et al. 2009) and provide added support for the hypothesis that early-life exposure to certain endocrine disruptors, even at low concentrations, may play a role in the current obesity epidemic. Given the widespread detection of PFOA in humans and wildlife and observed increase in related perfluorinated compounds of similar biological potential (Harada et al. 2011; Haug et al. 2009b), it is of considerable public health importance to understand and eliminate pathways of human exposures to PFAAs.

References


Prenatal exposure to PFOA and offspring overweight


