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Perfluorochemicals and Human Semen Quality: The LIFE Study

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BACKGROUND: The relation between persistent environmental chemicals and semen quality is evolving, although limited data exist for men recruited from general populations.

OBJECTIVES: We examined the relation between perfluorinated chemicals (PFCs) and semen quality among 501 male partners of couples planning pregnancy.

METHODS: Using population-based sampling strategies, we recruited 501 couples discontinuing contraception from two U.S. geographic regions from 2005 through 2009. Baseline interviews and anthropometric assessments were conducted, followed by blood collection for the quantification of seven serum PFCs (perfluorosulfonates, perfluorocarboxylates, and perfluorosulfonamides) using tandem mass spectrometry. Men collected a baseline semen sample and another approximately 1 month later. Semen samples were shipped with freezer packs, and analyses were performed on the day after collection. We used linear regression to estimate the difference in each semen parameter associated with a one unit increase in the natural log–transformed PFC concentration after adjusting for confounders and modeling repeated semen samples. Sensitivity analyses included optimal Box-Cox transformation of semen quality end points.

RESULTS: Six PFCs [2-[(N-methyl-perfluorooctane sulfonamido) acetate (Me-PFOSA-AcOH), perfluoroheptanoate (PFHxS), perfluorooctanoate (PFOA), perfluorooctane sulfonate (PFOS), and perfluorooctanoic acid (PFOA)] were associated with 17 semen quality end points before Box-Cox transformation. PFOA was associated with smaller sperm head area and perimeter, a lower percentage of DNA stainability, and a higher percentage of bicryptic and immature sperm. PFHxS, PFNA, PFOA, and PFO were associated with a lower percentage of sperm with coiled tails.

CONCLUSIONS: Select PFCs were associated with certain semen end points, with the most significant associations observed for PFOS but with results in varying directions.


Introduction

Perfluorochemicals (PFCs) are a group of synthetic chemicals that have been used in many consumer products [Agency for Toxic Substances and Disease Registry (ATSDR) 2009]. The two highest-production PFCs in the United States are perfluorooctane-sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA), both of which are frequently detected in humans (ATSDR 2009; Kato et al. 2011). Other PFCs include perfluorohexane sulfonic acid (PFHxS), which is a member of the same chemical category as PFOS, and perfluorononanoic acid (PFNA), which is a member of the same chemical category as PFOA (U.S. Environmental Protection Agency 2009). Chemicals within a given PFC chemical category share similar chemical structures, making them stable and suitable for surface coating and protectant formulations for paper-packaging products, carpets, leather products, and textiles that repel water, grease, and soil among other uses (ATSDR 2009). Varying (in)direct sources of environmental exposure serve as routes for human exposure (Prevedouros et al. 2006) including ingestion of food and water, inhalation, and lactational transfer (Fromme et al. 2009). Two recent studies pointed to food consumption as the primary pathway of exposure to PFOS and PFOA (Kelly et al. 2009; Trudel et al. 2008), with an estimated daily uptake from food of 2–3 ng/kg (Fromme et al. 2009).

Because of their long half-lives, ranging from 3.5 to 7.3 years (Olsen et al. 2007), some PFCs remain in the environment and bioconcentrate in animals (Conder et al. 2008; Fromme et al. 2009; Kelly et al. 2007, 2009; Lau et al. 2007). PFCs are not lipophilic, but they do bind to serum albumin (Han et al. 2003), which facilitates their measurement in serum and is thus indicative of long-term exposure (Fromme et al. 2009).

For the most part, well-designed epidemiologic research focusing on environmentally relevant concentrations of PFCs and human fecundity—the biologic capacity of men and women for reproduction (Buck Louis 2011)—has begun only recently. This lack of human research is in contrast to an evolving body of evidence in experimental animals that suggests altered male fecundity (decreased testosterone and increased estradiol levels in serum) in exposed rats and lower serum testosterone concentrations and epididymal sperm counts in exposed mice (Biegel et al. 1995; Shi et al. 2007; Wan et al. 2011). However, not all animal studies have reported evidence of adverse effects (Luebker et al. 2005).

Equivocal results have emerged from three distinct samples of men in whom selected PFCs were quantified in serum or plasma along with varying semen analyses: men from the general Danish population (Joensen et al. 2009, 2013), male partners of pregnant women (Specht et al. 2012; Toft et al. 2012), and couples seeking infertility treatment (Raymer et al. 2012). Joensen et al. (2009) observed negative associations for the highest PFOA and PFOS concentrations relative to the lowest and for the median number of normal spermatozoa in the general Danish population. Toft et al. (2012) reported negative associations for an increasing percentage of defect in sperm cell morphology in relation to serum PFOS concentrations among male partners of pregnant women from two European countries, but not among Inuit men, all of whom participated in the INUENDO Study. No associations were reported by Specht et al. (2009).
Buck Louis et al. (2012) for serum PFOA, PFOS, PFHxS, or PFNA and DNA damage or apoptotic sperm cells in men from the INUENDO Study. In a recent cross-sectional study, Raymer et al. (2012) reported no significant associations of plasma and semen PFOS and PFOA concentrations with reproductive hormones or select semen quality end points among 256 men attending infertility clinics; these authors did not consider either morphology or DNA fragmentation. In a study involving 247 young men being considered for military service in Denmark, Joensen et al. (2013) reported only one statistically significant negative association between perfluoro-1-heptanesulfonate and progressively motile sperm, although they did observe several negative relations between PFOS and serum total and free testosterone, free androgen index and other hormonal ratios (i.e., testosterone/luteinizing hormone; testosterone/estradiol; free testosterone/luteinizing hormone; free androgen index/luteinizing hormone).

This existing body of evidence is largely limited to assessment of a few PFCs (i.e., PFOA and PFOS) in male partners of pregnant women or of couples seeking infertility treatment. To our knowledge, there has been no attempt to assess PFCs in relation to a wide range of semen quality parameters among men from the general population, in particular in the United States. Thus, we examined the relation between PFCs and semen quality among 501 male partners of couples planning pregnancy.

Methods

Study design and cohort. We used the LIFE Study cohort for assessing seven PFCs in relation to 35 semen quality parameters in an attempt to explore possible associations. Briefly, 501 couples discontinuing contraception for the purposes of becoming pregnant were recruited from 16 counties in Michigan and Texas. Given the absence of established population-based sampling frameworks for identifying couples planning pregnancy (Buck et al. 2004), we utilized a marketing database in Michigan and the fishing/hunting license registry in Texas to ensure a sufficiently large denominator; couples planning pregnancy have been estimated to make up approximately 1% of the population (Buck et al. 2004; Slama et al. 2006). Forty-two percent of eligible couples enrolled in the study, as described elsewhere (Buck Louis et al. 2011). Inclusion criteria were minimal: Male partners needed to be at least 18 years of age, in a committed relationship, and without medically confirmed infertility and able to communicate in English or Spanish.

Data and biospecimen collection. Research assistants traveled to participants’ homes for the collection of data and biospecimens. Specifically, males completed baseline interviews, followed by a standardized anthropometric assessment for the determination of body mass index (BMI). After completion of the interview, blood collection equipment determined to be free of the environmental chemicals under study was used to obtain 10 cc of blood. Blood samples were transported on ice to the laboratory for processing; 2 mL of serum was used for the analysis of PFCs. Full human subjects approval was obtained from all participating institutions, and all participants provided written informed consent prior to enrollment into the study.

After enrollment in the study, men provided two semen samples approximately 1 month apart. Specimens were obtained via masturbation without the use of lubricants. Following a 2-day abstinence period, men obtained specimens via masturbation, without the use of lubricants, using at-home collection kits (Royster et al. 2000). Each kit included a glass collection jar with an attached button thermometer to monitor temperature every half hour throughout the process, a glass sperm migration straw (Vitrotubes 3520; VitroCom Inc., Mountain Lakes, NJ) containing hyaluronic acid and plugged at one end, and packing materials for shipping. Men were instructed to collect the semen sample in the jar, place the sperm migration straw into the jar (as an exploratory marker of sperm motility and viability at the time of collection), and to record on the label the time of last ejaculation and any spillage. When the specimen was ready for shipment, the men called a toll-free hotline to report sending their semen samples. Specimens were shipped in insulated shipping containers containing ice packs via overnight carrier and the second semen sample was obtained to corroborate azoospermia observed in the first sample, after which the male was advised to seek clinical care. An abbreviated semen analysis was performed on the second sample (i.e., volume, concentration, next-day motility, and sperm head morphology).

Toxicologic analysis. All analyses were conducted by the Division of Laboratory Sciences at the National Center for Environmental Health, Centers for Disease Control and Prevention (Atlanta, GA), using established protocols for the quantification of seven PFCs: 2-(N-ethyl-perfluoroctane sulfonamido) acetate (Et-PFOSA-AcOH), 2-(N-methyl-perfluoroctane sulfonamido) acetate (Me-PFOSA-AcOH), perfluoro-decanoate (PFDa), perfluorononanoate (PFNA), perfluorooctane sulfonamide (PFOSA), perfluorooctane sulfonate (PFOS), and perfluorooctanoic acid (PFOA).
Statistical analysis. In the descriptive phase of analysis, we assessed geometric means (GMs) and 95% confidence intervals (CIs) for PFCs by site using the nonparametric Wilcoxon test. In the analytic phase, we used linear mixed models to estimate the difference in each semen quality parameter associated with a one-unit change in the natural log (ln)-transformed concentration after adjusting to each PFC concentration. This method accounts for the correlation stemming from the use of up to two semen samples per male participant for the select end points measured in both samples (i.e., volume, concentration, next-day motility, and sperm head morphology). Of the 473 men, 378 (80%) provided two semen samples. We ran separate models for each PFC and semen parameter, and estimated beta coefficients (β) and 95% CIs for each model. Specifically, beta coefficients denoted the difference in each semen outcome per unit increase in each PFC. We adjusted a priori for age (years), BMI (weight in kilograms divided by height in meters squared), smoking (serum cotinine > 40.35 ng/mL or active smoking), abstinence time (days), sample age (hours), and study site (Carlsten et al. 2004; Jeemon et al. 2010; Jensen et al. 1998; Li et al. 2011; Ramlau-Hansen et al. 2007; Sadeu et al. 2010; Schmid et al. 2013). We conducted sensitivity analyses using Box-Cox analysis to determine the optimal transformation for each semen variable. We found that semen end points required ln transformation (n = 14), cubic root transformation (n = 6), or no (n = 14) transformation using the Shapiro-Wilk W statistic to assess all semen quality end points (Handelsman 2002). We also visually assessed the residual plots to affirm normality assumptions. Consistent with the exploratory nature of this work in light of limited data, we did not adjust for multiple comparisons. p-Values < 0.05 were considered statistically significant.

Results
A serum sample and at least one semen sample were available for 462 (92%) men. Eleven men had no semen sample, and 2 men had neither sample. The study cohort comprised mostly white non-Hispanic college-educated men with a mean (± SD) age of 31.8 ± 4.9 years and a mean BMI of 29.8 ± 5.6, with no significant differences by enrollment site (Table 1). Many of the men (57%) had previously fathered a pregnancy and few (17%) were current smokers. Mean (± SD) abstinence times for semen samples one and two were 4.0 ± 4.5 and 4.3 ± 5.6 days, respectively. Only 2 men (0.4%) reported an abstinence time < 2 days for the initial sample, as did 10 men (2.7%) who provided a second sample.

Table 2 presents the distributions for the seven PFCs by research site. Most of the chemicals were readily detected in men’s serum except for Et-PFOSA-AcOH and PFOA, for which 97% and 84% of concentrations, respectively, were < LOD. We observed no statistically significant difference in PFC concentrations between men who did or did not provide a semen sample, except for a higher PFNA concentration in men without a semen sample (GM = 1.82 ng/mL; 95% CI: 1.52, 2.18) compared with those who provided a semen sample (GM = 1.50 ng/mL; 95% CI: 1.43, 1.58) (see Supplemental Material, Table S1). Correlation coefficients between PFCs were low (range, 0.02–0.6), except for PFNA and PFDeA (r = 0.8), PFNA and PFOS (r = 0.7), and PFOS and PFDeA (r = 0.7). When each PFC and semen parameter were modeled individually, we observed several significant associations, some of which were suggestive of diminished semen quality (Table 3). Et-PFOSA-AcOH was the only PFC not associated with any semen quality parameter; however, data for Et-PFOSA-AcOH are difficult to interpret because concentrations were < LOD in 97% of samples. In the primary analysis or without Box-Cox transformation, three semen quality end points were associated with two or more PFCs: a) a reduction in the percentage of sperm with coiled tail (PFDeA, PFNA, PFOA, and PFOS); b) a reduction in the percentage of sperm with high DNA stainability (MePFOSA-AcOH and PFOS); and c) an increase in the number of immature sperm (MePFOSA-AcOH and PFOA). Other semen quality parameters were significantly associated with individual PFCs, but without a clear pattern.

Of the seven PFCs examined, PFOS, MePFOSA-AcOH, and PFOA were most often observed to be associated with semen quality end points, with 5, 3, and 2 separate associations, respectively. Specifically, a 1-unit increase in ln-transformed PFOS was associated with smaller sperm head area (β = −2.295; 95% CI: −4.052, −0.538), smaller sperm perimeter (β = −1.252; 95% CI: −2.276, −0.228), lower percentage of sperm with high DNA stainability (β = −15.153; 95% CI: −26.559, −3.747), higher percentage of bicephalic sperm (β = 4.127; 95% CI: 0.149, 8.105), and higher numbers of immature sperm.
Buck Louis et al.

Me-PFOSA-AcOH was associated with a higher percentage of sperm with neck/midpiece abnormalities ($\beta = 5.011$; 95% CI: 4.665, 5.348). In sensitivity analyses, 16 of 17 significant ($p < 0.05$) associations were observed, 15 of which were observed in the primary analysis (i.e., volume was not significant in the sensitivity analysis).

### Discussion

Findings of the present study suggest that select PFCs at environmentally relevant concentrations may be adversely associated with semen quality, with the exception of Et-PFOSA-AcOH, for which only 3% of concentrations were LOD. Associations suggestive of diminished semen quality included differences in sperm head (increased bicephalic) and morphology (increased immature sperm). Interpretation of these findings is uncertain, given the lack of well-established clinical norms for many individual parameters and because of reliance on next-day semen analysis and possible spurious associations. Morphologic sperm characteristics, including those involving the tail, may provide information about underlying mechanisms during the maturation process and eventual fertility, particularly in the context of other biochemical markers (Durutovic et al. 2013). In addition, each of these PFCs was associated with other semen characteristics, underscoring their varying patterns. Of the PFCs tested, PFOS, a precursor to PFOS, was significantly associated with the most semen parameters, including an increased percentage of bicephalic sperm and the number of immature sperm, both suggestive of diminished semen quality. However, we recognize the absence of established levels between normal sperm head morphology and genetic quality of spermatozoa (Ryu et al. 2001; Simon and Lewis 2011), limiting further speculation regarding our findings. We did not observe evidence of sperm DNA fragmentation on the basis of SCSA findings, which indicated a lower percentage of damaged sperm irrespective of PFC. It is important to note that only 16% of PFOSA concentrations were above the LOD, although quantification of PFCs was blinded to semen quality. The low prevalence of such exposure, with most of the measured concentrations below the LOD, is consistent with PFOSA’s discontinued production in the United States. The lack of consistent associations with motility—other than two positive associations for percent motility and sperm number—may reflect our reliance on next-day analysis, which provides only an exploratory assessment of viability and motility at the timing of collection absent validation methods.

Our findings suggest a negative association between select PFCs and sperm

### Table 3

<table>
<thead>
<tr>
<th>Semen parameter</th>
<th>Et-PFOSA-AcOH $\beta$ (95% CI)</th>
<th>Me-PFOSA-AcOH $\beta$ (95% CI)</th>
<th>PDefA $\beta$ (95% CI)</th>
<th>PFNA $\beta$ (95% CI)</th>
<th>PFOS $\beta$ (95% CI)</th>
<th>PFD $\beta$ (95% CI)</th>
<th>PFOSA $\beta$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General characteris$^a$</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Semen volume (mL)</td>
<td>$-0.952$ ($-1.837$, 0.933)</td>
<td>$-0.550$ ($-1.118$, 0.018)</td>
<td>$0.630$ ($-0.195$, 1.455)</td>
<td>$0.093$ ($-0.388$, 0.574)</td>
<td>$-0.092$ ($-0.457$, 0.273)</td>
<td>$0.058$ ($-0.197$, 0.312)</td>
<td>$-1.433$ ($-4.628$, 1.760)</td>
</tr>
<tr>
<td>Sperm viability (%)$^b$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sperm count ($\times 10^6$/mL)</td>
<td>$18.873$</td>
<td>$-9.951$</td>
<td>$81.003$</td>
<td>$45.125$</td>
<td>$0.679$</td>
<td>$9.741$</td>
<td>$130.776$</td>
</tr>
<tr>
<td>Sperm concentration ($\times 10^6$/mL)</td>
<td>$14.848$</td>
<td>$8.200$</td>
<td>$-1.063$</td>
<td>$5.218$</td>
<td>$0.388$</td>
<td>$0.025$</td>
<td>$47.187$</td>
</tr>
<tr>
<td>Sperm motility$^c$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Average path velocity ($\mu$m/sec)</td>
<td>$2.153$</td>
<td>$-0.106$</td>
<td>$3.761$</td>
<td>$2.293$</td>
<td>$2.223$</td>
<td>$0.378$</td>
<td>$9.433$</td>
</tr>
<tr>
<td>Straight line velocity ($\mu$m/sec)</td>
<td>$-2.380$</td>
<td>$-0.145$</td>
<td>$2.947$</td>
<td>$2.118$</td>
<td>$1.614$</td>
<td>$0.846$</td>
<td>$1.257$</td>
</tr>
<tr>
<td>Curvilinear velocity ($\mu$m/sec)</td>
<td>$0.151$</td>
<td>$-0.664$</td>
<td>$4.773$</td>
<td>$3.139$</td>
<td>$4.982^*$</td>
<td>$0.293$</td>
<td>$16.779$</td>
</tr>
<tr>
<td>Amplitude head displacement (μm)</td>
<td>$-0.372$</td>
<td>$-0.328$</td>
<td>$0.419$</td>
<td>$0.176$</td>
<td>$0.165$</td>
<td>$-0.086$</td>
<td>$-0.354$</td>
</tr>
<tr>
<td>Beat cross frequency (Hz)</td>
<td>$-2.662$</td>
<td>$-0.736$</td>
<td>$0.608$</td>
<td>$0.542$</td>
<td>$1.374$</td>
<td>$-0.136$</td>
<td>$-3.545$</td>
</tr>
<tr>
<td>Straigthness (%)</td>
<td>$-2.324$</td>
<td>$-0.218$</td>
<td>$1.304$</td>
<td>$0.233$</td>
<td>$1.299$</td>
<td>$-0.196$</td>
<td>$-17.583$</td>
</tr>
<tr>
<td>Percent motility (%)</td>
<td>$-0.335$</td>
<td>$-0.501$</td>
<td>$-0.932$</td>
<td>$0.928$</td>
<td>$1.473$</td>
<td>$1.556$</td>
<td>$-4.190$</td>
</tr>
<tr>
<td>Sperm head$^d$</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Length ($\mu$m)</td>
<td>$-0.145$</td>
<td>$-0.029$</td>
<td>$0.015^*$</td>
<td>$0.064$</td>
<td>$0.037$</td>
<td>$0.029$</td>
<td>$-0.509$</td>
</tr>
<tr>
<td>Area ($\mu$m$^2$)</td>
<td>$-0.271$</td>
<td>$-0.042$</td>
<td>$0.007$</td>
<td>$0.001$</td>
<td>$-0.201$</td>
<td>$-0.156$</td>
<td>$-229^*$</td>
</tr>
<tr>
<td>Width ($\mu$m)</td>
<td>$0.006$</td>
<td>$-0.105$</td>
<td>$0.270$</td>
<td>$0.212$</td>
<td>$0.066$</td>
<td>$-0.066$</td>
<td>$-1.252^*$</td>
</tr>
<tr>
<td>Perimeter ($\mu$m)</td>
<td>$-0.249$</td>
<td>$-0.068$</td>
<td>$0.022$</td>
<td>$-0.270$</td>
<td>$-0.116$</td>
<td>$-0.066$</td>
<td>$0.212$</td>
</tr>
<tr>
<td>Elongation factor (%)</td>
<td>$-0.295$</td>
<td>$-0.545$</td>
<td>$0.021$</td>
<td>$0.140$</td>
<td>$0.100$</td>
<td>$0.000$</td>
<td>$0.121$</td>
</tr>
<tr>
<td>Acrosome area of head (%)</td>
<td>$2.457$</td>
<td>$1.140$</td>
<td>$1.367$</td>
<td>$1.405$</td>
<td>$1.304^*$</td>
<td>$0.288$</td>
<td>$9.785$</td>
</tr>
</tbody>
</table>
PFCs and semen quality

Table 3. Continued.

<table>
<thead>
<tr>
<th>Semen parameter</th>
<th>E1-PFOSA-AcOH (β [95% CI])</th>
<th>Me-PFOSA-AcOH (β [95% CI])</th>
<th>PFDeA (β [95% CI])</th>
<th>PFNA (β [95% CI])</th>
<th>PFOA (β [95% CI])</th>
<th>PFOS (β [95% CI])</th>
<th>PFOSA (β [95% CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Straw: Distance (mm)*</td>
<td>-1.439 (95% CI: -7.612, 4.734)</td>
<td>0.649 (95% CI: -2.226, 3.522)</td>
<td>2.727 (95% CI: -1.166, 6.621)</td>
<td>-0.536, 4.019</td>
<td>-0.001</td>
<td>1.231*</td>
<td>13.890</td>
</tr>
<tr>
<td>Sperm morphology*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent normal, strict criteria</td>
<td>4.816 (95% CI: -4.735, 14.367)</td>
<td>-0.385</td>
<td>4.914 (95% CI: -0.829, 10.658)</td>
<td>3.897*</td>
<td>1.916</td>
<td>1.720</td>
<td>18.709</td>
</tr>
<tr>
<td>Percent normal, WHO criteria</td>
<td>6.098 (95% CI: 5.728, 17.920)</td>
<td>-0.432</td>
<td>5.799 (95% CI: -1.313, 12.912)</td>
<td>3.798 (95% CI: -0.168, 8.104)</td>
<td>1.726</td>
<td>1.835</td>
<td>25.417</td>
</tr>
<tr>
<td>Amorphous (%)</td>
<td>-14.484 (95% CI: -3.674, 5.635)</td>
<td>0.981 (95% CI: -6.698, 8.627)</td>
<td>-5.080 (95% CI: -2.066, 2.237)</td>
<td>-0.372</td>
<td>-0.020</td>
<td>0.162</td>
<td>-1.074</td>
</tr>
<tr>
<td>Round (%)</td>
<td>-1.309 (95% CI: -2.832, 0.213)</td>
<td>0.056</td>
<td>0.365 (95% CI: -0.555, 1.285)</td>
<td>0.311</td>
<td>-0.020</td>
<td>0.162</td>
<td>-1.074</td>
</tr>
<tr>
<td>Pyriform (%)</td>
<td>-0.248 (95% CI: -0.744, 0.259)</td>
<td>1.605</td>
<td>-0.012 (95% CI: -0.224, 0.846)</td>
<td>-0.416, 0.377</td>
<td>-0.049</td>
<td>-0.632</td>
<td>-1.376</td>
</tr>
<tr>
<td>Bicephalic (%)</td>
<td>-6.234 (95% CI: -2.803, 5.579)</td>
<td>-1.000 (95% CI: -5.21, 2.000)</td>
<td>-2.113, 0.209</td>
<td>-2.013, 1.096</td>
<td>-1.714, 0.469</td>
<td>-16.212, 13.459</td>
<td></td>
</tr>
<tr>
<td>Tapered (%)</td>
<td>-0.186 (95% CI: -1.800, 1.427)</td>
<td>0.283 (95% CI: -0.653, 0.169)</td>
<td>0.189</td>
<td>0.325</td>
<td>0.205</td>
<td>4.127*</td>
<td></td>
</tr>
<tr>
<td>Megahead (%)</td>
<td>-3.844 (95% CI: -1.746, 1.170)</td>
<td>-0.228 (95% CI: -0.932, 0.830)</td>
<td>-0.352</td>
<td>-0.392</td>
<td>-0.257</td>
<td>-1.085</td>
<td></td>
</tr>
<tr>
<td>Micro head (%)</td>
<td>-0.732 (95% CI: -2.528, 1.064)</td>
<td>0.088</td>
<td>-0.632</td>
<td>-0.355</td>
<td>-0.392</td>
<td>-0.257</td>
<td>-1.085</td>
</tr>
<tr>
<td>Neck or midpiece abnormalities (%)</td>
<td>-0.185 (95% CI: -1.885, 1.535)</td>
<td>0.114</td>
<td>-0.019</td>
<td>-0.214</td>
<td>-0.084</td>
<td>0.555</td>
<td></td>
</tr>
<tr>
<td>Coiled tail (%)</td>
<td>-0.376 (95% CI: -1.758, 0.954)</td>
<td>-0.026 (95% CI: -0.766, 0.710)</td>
<td>-0.064</td>
<td>-0.091</td>
<td>-0.351</td>
<td>-0.112</td>
<td>-0.327</td>
</tr>
<tr>
<td>Other tail abnormalities (%)</td>
<td>-0.185 (95% CI: -0.453, 0.351)</td>
<td>0.114</td>
<td>-0.019</td>
<td>-0.214</td>
<td>-0.084</td>
<td>0.555</td>
<td></td>
</tr>
<tr>
<td>Cytoplasmic droplet (%)</td>
<td>-0.949 (95% CI: -6.000, 4.103)</td>
<td>-1.277 (95% CI: -4.082, 0.231)</td>
<td>-0.123</td>
<td>-0.348</td>
<td>-0.407</td>
<td>-9.053</td>
<td></td>
</tr>
<tr>
<td>Immature sperm (%)</td>
<td>-4.963 (95% CI: 18.719, 2.610)</td>
<td>0.362</td>
<td>2.610</td>
<td>0.411</td>
<td>2.096</td>
<td>30.881*</td>
<td></td>
</tr>
<tr>
<td>Sperm chromatin stabilitya</td>
<td>-2.134 (95% CI: 11.246, 5.119)</td>
<td>-1.695, 3.501</td>
<td>-6.243, 2.873</td>
<td>-3.136, 8.355</td>
<td>-4.668, 3.846</td>
<td>-0.889, 0.070</td>
<td>51.266, 130.496</td>
</tr>
</tbody>
</table>

Analysis includes 5 azoospermic men but excludes 39 men who had missing values for PFOS (n = 11), missing semen samples (n = 26), or both (n = 2). Fixed-effects and mixed-effects models were used to analyze semen parameters with one and two measurements, respectively. PFC concentrations were ln-transformed and adjusted for age (years), BMI (kg/m²), serum cotinine (active smoking yes/no), abstinence (days), sample age (hours), and research site (Texas/Michigan).

*aAssessed in both semen samples. **Assessed by SCSA® analysis only in the baseline semen sample. Rothmann et al. (2013). *WHO (1992). *p < 0.05. **p < 0.01.
Conclusions
We found that select PFCs at environmentally relevant concentrations were associated with differences in sperm head, morphology, and DNA characteristics, including differences indicative of higher and lower semen quality. These exploratory findings suggest some deleterious differences in sperm morphology (e.g., immature, bicephalic) but await corroboration. Follow-up investigation of the impact of semen changes on male reproductive health or couple fecundity is needed, including in-depth semen analyses.

References


