Persistent organochlorines, sedentary occupation, obesity and human male subfertility

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BACKGROUND: Studies have suggested that the quality of human semen has been declining over recent decades, presumably because of lifestyle or environmental factors. METHODS: Polychlorinated biphenyls and organochlorine pesticides were analysed in the plasma of 25 men with poor semen quality, 20 men with normal semen quality and idiopathic subfertility and 27 men with normal semen quality and female factor subfertility. Samples of seminal fluid were also analysed to assess the relationship between the levels in blood and semen. RESULTS: The results indicate no difference in the levels of organochlorines between the groups. The levels of organochlorines in seminal fluid were proportional to the levels in plasma, but ~40 times lower. Men with poor semen quality were three times more likely to be obese than men with normal semen quality. There was also a significant negative correlation between semen quality parameters and body mass index among men with normal semen quality. The prevalence of sedentary work was lowest among men with the best semen quality. CONCLUSIONS: Poor semen quality was found to be associated with sedentary work and obesity but not with plasma levels of persistent organochlorines. More research is needed to assess whether sedentary lifestyle and obesity are causal factors in the decline of semen quality.

Key words: male fertility/obesity/organochlorines/sedentary work/semen quality

Introduction
Several studies have suggested that the quality of human semen has been declining over recent decades (Carlsen et al., 1992; Auger et al., 1995; Adamopoulos et al., 1996; Irvine et al., 1996). Although studies have also been contradictory (Bujan et al., 1996; Fisch et al., 1996b; Paulsen et al., 1996), indicating that these changes have not taken place in all parts of the world, this has aroused concern about male fertility in the future. Geographical differences in semen quality (Fisch et al., 1996a; Jorgensen et al., 2001) also support the idea that semen quality may have decreased in some areas. Fertility, measured as time to pregnancy, is lower in areas where population semen quality is lower than in areas of higher population semen quality (Joffe, 1996). These alleged changes in semen quality appear to be recent (Carlsen et al., 1992; Auger et al., 1995; Adamopoulos et al., 1996; Irvine et al., 1996) which may indicate a link with lifestyle or environmental factors such as increased levels of environmental pollutants.

Among the environmental pollutants identified as potential causes of decreased quality of human semen are persistent organochlorines, which have been used as pesticides or industrial chemicals. These chemicals are stable and can reach high concentrations in humans and animals that are at high levels of the food chain and the exposure takes place throughout life. Many organochlorines have hormone-disrupting properties and are therefore suspected candidates for affecting fertility (Sharpe and Skakkebaek, 1993; Toppari et al., 1996; Sharpe, 2003). It has been hypothesized that various human male reproductive disorders, such as testicular germ cell cancer, cryptorchidism, hypospadias and low sperm counts, now collectively termed ‘testicular dysgenesis syndrome’, have a common aetiology and may be related to increased estrogen exposure in utero (for review see Sharpe, 2003). Although susceptibility to hormone disruption is probably highest in the pre-, peri- and postnatal periods, spermatogenesis during adulthood is also hormone-regulated and may therefore be affected as well. The negative feedback of androgens on gonadotrophin secretion is for example currently employed for male contraception and a major component of this action is mediated via aromatization to estrogen (O’Donnell et al., 2001). Estrogen also plays a role in the resorption of fluid in the rete testis, which concentrates the sperm as they enter the epididymis (O’Donnell et al., 2001). Rete testis might thus also be a site of hormone disruption potentially leading to poor semen quality. In vitro studies have shown that the organochlorine pesticide γ-hexachlorocyclohexane (γ-HCH) has the ability to induce membrane depolarization in human...
sperm and modify the sperm responsiveness to progesterone, a physiological agonist of the acrosome reaction (Silvestroni and Palleschi, 1999) and that sperm from men exposed to polychlorinated biphenyls (PCB) and polychlorinated dibenzofurans have reduced capacity to penetrate hamster oocytes compared to sperm from non-exposed men (Guo et al., 2000). Deteriorating effects on male fertility without apparent effects on semen parameters should therefore also be considered.

Obesity is becoming increasingly prevalent worldwide (Sorensen, 1988; Seidell, 1997; Visscher and Seidell, 2001; Friedrich, 2002) and is now considered to be one of the most important health concerns in many countries. It has been associated with an increased risk of many serious illnesses such as cardiovascular diseases, diabetes mellitus and some types of cancer (Visscher and Seidell, 2001). Adipose tissue is an important site of steroid production and metabolism, and obesity has been associated with reproductive disorders in women, including menstrual abnormality, infertility, miscarriage, and reduced success of assisted reproduction (Norman and Clark, 1998). There are few data on reproductive outcomes in the obese male, but some studies have shown lower plasma levels of sex hormone-binding globulin (SHBG), total testosterone, free testosterone and FSH in obese men compared to non-obese men (Strain et al., 1982; Haffner et al., 1993).

The increasing prevalence of obesity is believed to be caused largely by an environment characterized by a variety of convenient, relatively inexpensive, energy-dense food, coupled with advances in technology and transportation that reduce the need for physical activity. Recent studies have shown that sedentary position at work results in higher scrotal temperature (Hjollund et al., 2002a), which has been shown to have negative effects on semen quality (Hjollund et al., 2002b), although direct effects of sedentary work position on semen quality were not established.

The aim of this study was to determine if organochlorine levels are associated with male fertility, either via spermatogenesis or via other pathways without apparent effects on semen. We also examined the association of sedentary work and obesity with semen quality.

Materials and methods

Study population

Men who contacted the Department of Assisted Reproduction at the Landspitali University Hospital of Iceland from March 1999 to May 2001 and fitted into one of the following groups, based on previous semen analyses, were selected for the study. This clinic serves the entire population of Iceland and services of assisted reproduction are offered nowhere else in the country. Male factor subfertility group (MFS): men with poor semen quality (two or more of the following required: sperm concentration ≤10 × 10^6/ml and/or total sperm count ≤20 × 10^6 and/or progressive sperm motility ≤30%) and no marked clinical or pathological disorders. Idiopathic subfertility group (IS): men with ‘normal’ or better semen quality (sperm concentration ≥20 × 10^6/ml and/or total sperm count ≥40 × 10^6 and progressive sperm motility ≥40%) and unexplained subfertility. Female factor subfertility group (FFS): men with ‘normal’ or better semen quality (sperm concentration ≥20 × 10^6/ml and/or total sperm count ≥40 × 10^6 and progressive sperm motility ≥40%) whose spouses had a known fertility problem, such as closed Fallopian tubes. A total of 72 men were recruited, 25 in the MFS group, 20 in the IS group and 27 in the FFS group. Participation rate was >90% in all groups. The study was approved by the Ethics Committee of the Landspitali University Hospital and all participants signed an informed consent form.

Sample collection

The participants filled in a questionnaire regarding their weight, height, age and some lifestyle factors, such as diet, smoking and occupation. A blood sample was drawn into a 10 ml glass-vacutainer containing EDTA, centrifuged and the plasma stored at −20°C until analysed for organochlorine concentrations. Semen samples were obtained after a recommended period of 3–5 days sexual abstinence. Samples from the first 20 men who joined the study (seven from the MFS group, four from the IS group and nine from the FFS group) were also stored at −20°C for analysis of organochlorine concentrations, after removal of sperm by centrifugation.

Semen quality

All semen samples were analysed according to World Health Organization (1999) guidelines as a part of usual routine of the clinic. Sperm concentration was determined by an improved Neubauer haemocytometer and sperm motility was assessed by direct observation under a microscope by an experienced laboratory specialist.

Organochlorine analysis

The samples (2.5–5 g) were extracted according to the method of Luotamo et al. (1985). Recovery was followed by the addition of e-HCH, α,α′-dichlordiphenyl dichloroethane (α,α′-DDD) and PCB nos. 112 and 198 (no. according to IUPAC) to all samples at the first step of extraction. Clean-up was accomplished with concentrated sulphuric acid. Fourteen chlorinated pesticides or their metabolites [hexachlorobenzene (HCB), α-, β- and γ-HCH, α- and γ-chlordane, trans-nonachlor, oxychlordane, three toxaphene congeners (Parlar no. 26, 50 and 62), p,p′-dichlordiphenyl dichloroethene (p,p′-DDE), p,p′-DDD, p,p′-dichlordiphenyl trichloroethane (p,p′-DDE) and other congeners (IUPAC nos. 18, 28, 31, 33, 52, 66, 74, 99, 101, 105, 114, 118, 128, 138, 141, 149, 153, 156, 157, 167, 170. 180. 187, 189, 194 and 209)] were determined by gas chromatography (HP5890, series II), using two different capillary columns from J&W Scientific (DB5, 60 m, 0.25 mm inside diameter, 0.25 μm film thickness and DB1701, 60 m, 0.25 mm inside diameter, 0.25 μm film thickness) and an electron capture detector. Helium was used as the carrier gas and nitrogen as a make-up gas. Standard curves were made from the corresponding individual standards and an internal standard (1,2,3,4-tetrachloronaphthalene) from Promochem (Germany) or AccuStandard (USA). The PCB congeners and pesticides were analysed on both columns and the lower value reported.

Assessment of sedentary work

Participants were classified by physical activity at work into three groups (sedentary, active, indeterminate) using information on occupation. The classification was done by six researchers independently, and a majority agreement was required to classify the occupation as either sedentary (likely to sit down more than half of their working hour) or active (likely to sit down less than half of their working hour). The individuals classified as sedentary workers included for example administrators, office workers, civil engineers, educators, motor vehicle operators, a doctor, a lawyer and a student.
The individuals classified as active or non-sedentary workers included labourers, craftsmen, mechanics, store attendants, a physical education teacher and a daycare worker. Physical activity at work was classified as indeterminate for salesmen and production/operation managers.

**Statistics**

Body mass index (BMI), semen parameters and organochlorine levels were presented as medians or geometric means as these parameters were not normally distributed. These parameters were analysed using non-parametric tests or rank-transformed before applying statistical tests requiring normal distribution.

Fertility groups were compared by analysis of variance (ANOVA) (normally distributed variables) and the non-parametric Kruskal–Wallis test and/or the non-parametric Mann–Whitney test (non-normally distributed variables). Organochlorine levels were rank-transformed due to their skewed distribution and compared across fertility groups using analysis of covariance (ANCOVA), with BMI and/or age as covariates. Relationships between organochlorine levels, semen parameters, age and BMI were investigated using Spearman non-parametric correlation. When examining correlation between semen parameters and other parameters, the MFS group was not combined with the other two groups, as this group was selected on the basis of different semen parameters. The IS and the FFS groups were on the other hand selected on the basis of the same semen criteria, but the difference was only significant for progressive motility ($P = 0.04$). The difference in BMI across groups was reflected in more than three times higher prevalence of obesity, defined as BMI $\geq 30$ kg/m$^2$ by study group.

**Results**

The characteristics of the MFS, IS and FFS groups are presented in Table I. The mean age was $\sim 3.5$ years higher in the FFS group than in the IS and the MFS group. This difference was statistically significant ($P = 0.02$). BMI (kg/m$^2$) was significantly higher in the MFS group than in the FFS group ($P = 0.01$). No significant difference was found in the prevalence of smoking between the groups, and smoking did not correlate with any of the sperm parameters. As a result of the selection criteria, the sperm parameters in the MFS group were well below the World Health Organization (1999) reference values for normal semen. The men in the IS group tended to have poorer semen quality than the men in the FFS group, although selected on the same ‘normal’ semen quality criteria, but the difference was only significant for progressive motility ($P = 0.04$). The difference in BMI across groups was reflected in more than three times higher prevalence of obesity, defined as BMI $\geq 30$ kg/m$^2$, among men in the MFS group than in the IS and FFS groups (Figure 1).

Eight PCB congeners (IUPAC nos. 99, 118, 138, 153, 170, 180, 187 and 194) and the organochlorine pesticides HCB, $\beta$-HCH, trans-nonachlor and $p,p^\prime$-DDE were detected in all plasma samples. The toxaphene congener parlar 50, the pesticide metabolite oxychlordane and four additional PCB congeners (IUPAC nos. 74, 156, 167 and 183) were detected in $> 85\%$ of the plasma samples and were also included in the statistical analysis. Only $p,p^\prime$-DDE and PCB congeners nos. 153 and 180 were above detection limits in all the semen samples. The concentrations of these compounds are presented in Table II.

**Correlation between individual organochlorine congeners**

Very strong correlations were found between individual PCB congeners ($n = 72$, $r = 0.40–0.98$, $P < 0.000001–0.0001$).
Organochlorines, lifestyle and male fertility

Table II. Organochlorine levels (ng/g) of men in the three study groups

<table>
<thead>
<tr>
<th>Component</th>
<th>Total</th>
<th>MFS group</th>
<th>IS group</th>
<th>FFS group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 72)</td>
<td>(n = 25)</td>
<td>(n = 20)</td>
<td>(n = 27)</td>
</tr>
<tr>
<td>PCB-74</td>
<td>0.06 (0.02–0.20)</td>
<td>0.06 (0.02–0.12)</td>
<td>0.05 (0.02–0.20)</td>
<td>0.07 (0.03–0.15)</td>
</tr>
<tr>
<td>PCB-99</td>
<td>0.09 (0.03–0.42)</td>
<td>0.09 (0.04–0.26)</td>
<td>0.07 (0.03–0.42)</td>
<td>0.09 (0.04–0.26)</td>
</tr>
<tr>
<td>PCB-118</td>
<td>0.12 (0.03–0.64)</td>
<td>0.13 (0.05–0.33)</td>
<td>0.10³ (0.03–0.64)</td>
<td>0.14⁴ (0.04–0.47)</td>
</tr>
<tr>
<td>PCB-138</td>
<td>0.40 (0.14–1.90)</td>
<td>0.41 (0.18–1.03)</td>
<td>0.33³ (0.14–1.90)</td>
<td>0.44³ (0.21–1.27)</td>
</tr>
<tr>
<td>PCB-153</td>
<td>0.63 (0.22–3.05)</td>
<td>0.63 (0.27–1.42)</td>
<td>0.53³ (0.22–3.05)</td>
<td>0.70³ (0.36–1.71)</td>
</tr>
<tr>
<td>PCB-156</td>
<td>0.06 (0.02–0.22)</td>
<td>0.06 (0.02–0.12)</td>
<td>0.04⁴ (0.02–0.22)</td>
<td>0.07⁴ (0.02–0.12)</td>
</tr>
<tr>
<td>PCB-167</td>
<td>0.03 (0.01–0.09)</td>
<td>0.03 (0.01–0.07)</td>
<td>0.02 (&lt;0.02–0.06)</td>
<td>0.03 (&lt;0.02–0.09)</td>
</tr>
<tr>
<td>PCB-170</td>
<td>0.15 (0.05–0.63)</td>
<td>0.14 (0.06–0.30)</td>
<td>0.13³ (0.05–0.63)</td>
<td>0.18³ (0.11–0.30)</td>
</tr>
<tr>
<td>PCB-180</td>
<td>0.35 (0.12–1.51)</td>
<td>0.33 (0.14–0.63)</td>
<td>0.30 (0.12–1.51)</td>
<td>0.41 (0.23–0.69)</td>
</tr>
<tr>
<td>PCB-183</td>
<td>0.04 (0.02–0.22)</td>
<td>0.04 (0.02–0.12)</td>
<td>0.04 (0.02–0.22)</td>
<td>0.04 (0.02–0.13)</td>
</tr>
<tr>
<td>PCB-187</td>
<td>0.13 (0.04–0.82)</td>
<td>0.12 (0.05–0.38)</td>
<td>0.12 (0.04–0.82)</td>
<td>0.14 (0.07–0.44)</td>
</tr>
<tr>
<td>PCB-194</td>
<td>0.06 (0.02–0.29)</td>
<td>0.05 (0.02–0.14)</td>
<td>0.05⁴ (0.02–0.29)</td>
<td>0.07⁴ (0.04–0.14)</td>
</tr>
<tr>
<td>Σ12PCB</td>
<td>2.13 (0.77–9.95)</td>
<td>2.12 (0.89–4.66)</td>
<td>1.81 (0.77–9.95)</td>
<td>2.40 (1.38–5.30)</td>
</tr>
<tr>
<td>HCB</td>
<td>0.37 (0.15–0.77)</td>
<td>0.39 (0.15–0.77)</td>
<td>0.31 (0.15–0.83)</td>
<td>0.39 (0.18–0.87)</td>
</tr>
<tr>
<td>β-HCH</td>
<td>0.18 (0.05–0.56)</td>
<td>0.20 (0.05–0.56)</td>
<td>0.15 (0.05–0.43)</td>
<td>0.20 (0.07–0.70)</td>
</tr>
<tr>
<td>Oxychlordane</td>
<td>0.03 (&lt;0.01–0.20)</td>
<td>0.03 (&lt;0.02–0.14)</td>
<td>0.05 (&lt;0.01–0.20)</td>
<td>0.04 (&lt;0.02–0.12)</td>
</tr>
<tr>
<td>trans-Nonachlor</td>
<td>0.12 (0.04–0.75)</td>
<td>0.12 (0.04–0.46)</td>
<td>0.11 (0.05–0.75)</td>
<td>0.13 (0.04–0.49)</td>
</tr>
<tr>
<td>p,p'-DDE</td>
<td>1.13 (0.27–15.2)</td>
<td>1.08 (0.40–5.02)</td>
<td>1.10 (0.27–15.2)</td>
<td>1.21 (0.30–4.34)</td>
</tr>
<tr>
<td>Toxaphene*</td>
<td>0.04 (&lt;0.01–0.42)</td>
<td>0.05 (&lt;0.02–0.20)</td>
<td>0.04 (&lt;0.01–0.42)</td>
<td>0.05 (&lt;0.02–0.22)</td>
</tr>
<tr>
<td>Semen (n = 20)</td>
<td>(n = 7)</td>
<td>(n = 4)</td>
<td>(n = 9)</td>
<td></td>
</tr>
<tr>
<td>PCB-153</td>
<td>0.018 (0.010–0.060)</td>
<td>0.015 (0.010–0.022)</td>
<td>0.026 (0.011–0.060)</td>
<td>0.017 (0.010–0.032)</td>
</tr>
<tr>
<td>PCB-180</td>
<td>0.013 (0.010–0.027)</td>
<td>0.012 (0.010–0.021)</td>
<td>0.017 (0.011–0.027)</td>
<td>0.017 (0.005–0.032)</td>
</tr>
<tr>
<td>p,p'-DDE</td>
<td>0.022 (0.009–0.23)</td>
<td>0.017 (0.011–0.027)</td>
<td>0.039 (0.009–0.23)</td>
<td>0.022 (0.010–0.056)</td>
</tr>
</tbody>
</table>

Values are geometric means and range.

*P < 0.05 (rank-transformed organochlorine levels with body mass index (BMI) and/or age as covariates).

²P < 0.1 (rank-transformed organochlorine levels with BMI and/or age as covariates).

\*Parlar 50.

MFS = male factor subfertility; IS = idiopathic subfertility; FFS = female factor subfertility.

There were also correlations between individual pesticides (n = 72, r = 0.27–0.84, P < 0.000001–0.02) and between pesticides and PCB congeners (n = 72, r = 0.21–0.82, P < 0.000001–0.08).

Correlation of plasma organochlorine levels with age and BMI

Most of the organochlorines analysed showed a significant positive correlation with age. HCB, β-HCH, p,p'-DDE and some of the PCB congeners also correlated positively with BMI (Table III). However, no relationship was found between age and BMI (n = 72, r = 0.02, P = 0.90).

Comparison of organochlorine levels between the MFS, IS and FFS groups

The highest mean plasma levels of most of the organochlorines were found in the FFS group. However, it was not possible to compare the groups directly, as there was a significant difference in the mean age and BMI between the groups and the organochlorine levels correlated strongly with one or both factors. When the groups were compared with age and BMI as covariates, only PCB nos. 156 and 194 remained significantly different (P = 0.008 and P = 0.02 respectively) (Table II).

The mean levels of p,p'-DDE, PCB-153 and PCB-180 in semen were higher in the IS group than in the MFS and the FFS group, but the small sample size and a wide range of data did not allow any meaningful statistical comparison between the groups.

Relationship between organochlorine concentration in plasma and semen

A very strong correlation was found between p,p'-DDE concentration in plasma and the corresponding concentration in semen (r = 0.78, P < 0.0001). The correlation was also significant for PCB-153 (r = 0.45, P = 0.04), but not for PCB-180 (r = 0.38, P = 0.09). The concentrations in semen

![Table III. Correlation of organochlorine levels with age and body mass index (BMI)](image-url)
were on average ~ 40 times lower than the concentrations in plasma.

**Correlation of semen parameters with age**

A significant positive correlation was found between sperm motility and age in the MFS group ($r = 0.46$, $P = 0.02$) but this relationship was not observed among men with ‘normal’ semen quality (IS and FFS groups, $r = 0.09$, $P = 0.52$). Sperm concentration ($r = 0.47$, $P = 0.04$), sperm count ($r = 0.44$, $P = 0.05$) and progressively motile sperm count ($r = 0.46$, $P = 0.04$) showed a positive correlation with age among men with ‘normal’ semen quality and BMI < 25 kg/m$^2$ ($n = 20$), but the correlation disappeared when overweight and obese men (BMI $\geq 25$ kg/m$^2$) were included in the analysis ($r = -0.06$, $P = 0.68$; $r = 0.04$, $P = 0.81$; and $r = 0.05$, $P = 0.74$ respectively).

**Correlation of plasma PCB concentration and semen parameters among normal weight men**

No association was seen between plasma organochlorine levels and any of the semen parameters when data from all 72 subjects was examined (data not shown). When the data from normal weight men (BMI < 25 kg/m$^2$) with ‘normal’ semen quality (IS and FFS group) were examined separately, a significant positive correlation was found between PCB congener no. 170 and sperm concentration ($r = 0.46$, $P = 0.04$), sperm count ($r = 0.54$, $P = 0.01$) and progressively motile sperm count ($r = 0.48$, $P = 0.04$). This relationship was also significant for sperm count and PCB congeners no. 180 ($r = 0.52$, $P = 0.02$) and no. 194 ($r = 0.50$, $P = 0.02$).

**Relationship of semen parameters with sedentary work and BMI**

A statistically significant negative correlation between BMI and both sperm concentration and sperm count was observed among men with ‘normal’ semen quality (IS and FFS groups) ($r = -0.33$, $P = 0.02$; and $r = -0.30$, $P = 0.04$ for concentration and count, respectively) (Figure 2). The MFS group was analysed separately as this group was selected on the basis of poor semen quality whereas the IS and the FFS groups were selected on the same ‘normal’ semen quality criteria and could therefore be combined. In the MFS group a negative, but statistically non-significant, trend for sperm concentration ($r = -0.16$, $P = 0.43$) and sperm count ($r = -0.27$, $P = 0.19$) with increasing BMI was observed.

The prevalence of sedentary work was 60% among men with poor semen quality (MFS group) compared to 42% among men with ‘normal’ semen quality (IS and FFS groups). This difference was not significant ($P = 0.21$). When men with normal semen quality were split into ‘low normal’ and ‘high normal’ sperm concentration subgroups, sedentary work was significantly more common among men with the lower sperm concentration (59%) compared to the men with the higher sperm concentration (22%) ($P = 0.03$). The difference in the prevalence of sedentary work between the ‘high normal’ and ‘low normal’ concentration subgroups was observed both among men with BMI < 25 kg/m$^2$ and BMI $\geq 25$ kg/m$^2$ but was more pronounced in the leaner group (Figure 3).

**Discussion**

Few studies have reported the levels of organochlorines in seminal fluid. The levels of PCB-153, PCB-180 and p,p'-DDE in semen in our study were very similar to the levels found in a recent study from The Netherlands (Dallinga et al., 2002). The plasma organochlorine levels were somewhat higher in our study, leading to a plasma:semen ratio of ~40 on average compared to a ratio of ~20 in the Dutch study. Earlier studies (Bush et al., 1986; Schliebusch et al., 1989; Enslen et al., 1990) showed considerably higher levels in semen, but did not provide information on the plasma levels for comparison.
The fact that the presumably fertile men in the FFS group generally had the highest plasma organochlorine levels does not support the idea that the poor semen quality in the MFS group or the subfertility of the men in the IS group resulted from exposure to organochlorine compounds. We found a positive correlation between organochlorine levels and age, which is in agreement with results from others (Dallinga et al., 2002; Voorspoels et al., 2002), and accounts for the higher levels in the FFS group where the mean age is ~3.5 years higher than in the other two groups. We also found a positive correlation between PCB levels and semen parameters among normal weight men (BMI < 25 kg/m²), which is in agreement with results from Dallinga et al. (2002) who found a positive correlation between organochlorine levels and semen quality parameters. In our study, this correlation disappeared when overweight and obese men (BMI ≥ 25 kg/m²) were included in the analysis, indicating an inverse association with increased body fat. A likely explanation for this positive correlation between the PCB levels and semen parameters is the age-organochlorine relationship, because the PCB congeners mainly involved were the ones that showed the strongest correlation with age, and there was also a positive correlation between semen parameters and age. Nevertheless, it is difficult to explain the biological rationale for this observed positive correlation between semen parameters and age. A review of the literature on the association between male age and semen quality (Kidd et al., 2001) showed conflicting results, especially on sperm concentration, where five studies showed negative correlation between sperm concentration and age, six studies found little or no association, eight studies found positive correlation and two studies suggested an inverse U-shaped distribution, that is the youngest and oldest age groups had lower sperm concentration than the age groups in between. However, the possibility of positive effects of organochlorines on sperm production should perhaps also be considered as many of them have anti-androgenic or anti-estrogenic properties (Jansen et al., 1993; Krishnan and Safe, 1993; Sohoni and Sumpter, 1998; Arcaro et al., 2000) and could therefore hypothetically inhibit normal negative feedback of hormones on the pituitary, leading to increased hormone production in the testis. High serum DDE levels have been inversely correlated to semen volume and sperm count in Mexican men where DDT is still used for malaria control (Ayotte et al., 2001) and a significant decrease in fertility was seen among men exposed to pesticides in cotton fields in India (Rupa et al., 1991), which contradicts this idea, but the levels of exposure in these cases were extreme, and endocrine-disrupting chemicals can have opposite effects in low versus high doses (Alworth et al., 2002; Kohn and Melnick, 2002).

The observed positive correlation between some of the organochlorines and BMI has also been previously documented (Schildkraut et al., 1999; Pelletier et al., 2002), and could explain the elevated levels of some of the organochlorines in the MFS group compared to the men of similar age in the IS group. However, a few men in the IS group had very high plasma organochlorine levels, leading to much bigger ranges than in the other two groups, although this group had the lowest geometric mean. Elevated levels of organochlorines in semen samples from men with idiopathic subfertility compared to semen samples from men with pathological sperm findings have previously been reported (Ensslen et al., 1990), but the levels were 10–100 times higher than in our study. Obviously, there could be many different reasons for the idiopathic subfertility, some of them found in the female partner. Our study does not answer the question whether organochlorine exposure is one of the reasons, but the results indicate that if organochlorines are to blame, then it is only in a very limited number of cases at the levels found in Icelandic men. Unfortunately our sample size did not allow us to apply multivariate regression analyses to the rank-transformed values of organochlorine levels to assess their relationship with semen parameters while adjusting for important confounders, particularly age and BMI.

It has been shown (Seidell, 1997) that quite considerable increases in the prevalence of obesity (defined as BMI ≥ 30 kg/m²) can be the consequence of relatively minor changes in average body weight. In our study, a difference of 2.5 kg/m² in the average BMI resulted in more than three times higher prevalence of obesity (BMI ≥ 30 kg/m²) among men with poor semen quality (MFS group) compared to men with ‘normal’ semen quality (IS and FFS groups). There was also a significant downward trend in sperm concentration and sperm count with increasing BMI among men with semen quality in the ‘normal’ range, indicating negative influences of obesity and perhaps also overweight on sperm production. However, it is difficult to separate the effect of obesity from that of limited physical activity, as these two factors are likely to be highly associated. A physically demanding occupation has been shown to reduce the risk of obesity by 42% even without any leisure time physical activity (King et al., 2001). In our data, there is no significant association between sedentary work and overweight or obesity, but we do not have any information regarding leisure time activity. The use of self-reported weight and height for the calculation of BMI is not optimal. However, many studies have shown that most people are fairly accurate in reporting their weight and height, although misreporting may be increased in certain subgroups (Bolton-Smith et al., 2000; Kuczmaraki et al., 2001; Shapiro and Anderson, 2003). In our study the relative rather than absolute prevalence of obesity within the study population is of concern. Differential misreporting of height and weight between subgroups is unlikely as the possible association between BMI and semen quality was not known to the subjects at the time of data collection.

We found a higher prevalence of sedentary work among men with ‘low normal’ sperm concentration compared to those with ‘high normal’ sperm concentration. This difference was more pronounced among normal weight men (BMI < 25) than the heavier ones. These results may indicate a stronger relationship of sperm production with sedentary work, most likely through elevated scrotal temperature, than with obesity. However, our sample size is limited and all results should thus be interpreted with caution. Overweight and obesity could also contribute to the picture, possibly through modification of hormonal levels, as obesity has been
connected to mild hypogonadotrophic hypogonadism in men (Strain et al., 1982; Haffner et al., 1993). It can also be hypothesized that obesity could increase the hyperthermal effect of sedentary work on the testis, and in that way have indirect effects on semen quality.

Recently a new hypothesis to explain the global epidemic of obesity was introduced. It was suggested that environmental chemicals were responsible by interfering with the human weight control system and was pointed out that compounds such as dieldrin, γ-HCH and HCB have been reported to induce obesity in animals (Baillie-Hamilton, 2002). This hypothesis could fit in with our results that show a positive correlation between some of the organochlorines and BMI, but this correlation in cross-sectional data does not prove a causal relationship in humans. The higher levels of organochlorines at higher BMI could merely indicate a higher lifetime intake of fat-rich food with high organochlorine contamination, which results in overweight or obesity because of high energy content. However, it is also possible that altered hormone environment in utero could affect body fat distribution and risk of obesity in adulthood and predispose to sedentary lifestyle and favour the selection of a sedentary occupation. The organochlorine accumulation could also be the result of this predisposition to obesity.

In conclusion, we found decreased semen quality to be associated with sedentary work and obesity rather than the levels of persistent organochlorines. This study thus suggests that the decreased human semen quality over recent decades may be related to a change in living habits, characterized by a more sedentary lifestyle associated with high energy intake and increased prevalence of obesity, rather than increased exposure to organochlorines. Analytic epidemiological studies are needed to evaluate this further.

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