Prepubertal and Pubertal Predictors of Semen Quality in a Prospective Cohort Study of Russian Young Men: Focus on Endocrine Disrupting

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Background

We have a unique longitudinal study following a cohort of boys with prepubertal assessment of exposures to endocrine disrupters (EDCs) and annual follow-up of growth and puberty to evaluate semen quality.

Objective

To describe semen quality and explore associations of prepubertal serum 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) levels and pubertal measurements with semen parameters in a longitudinal cohort of Russian boys.

Study Population

- 516 8-9-year-old boys were enrolled from 2003 to 2005 and underwent annual growth and sexual development assessments ( Tanner staging and measurement of testicular volume) for ten years (total 4697 visits).
- At age 18 years, 302 subjects were eligible for semen sample collection.

Figure 1. Recruitment and recruitment for boys’ lumbar sample in Russian Children’s Study.

Methods

- The study was approved by the Human Studies Institutional Review Boards of the Chapayev Medical Association (Chapayev, Russia), HSPH and BWH (Boston, MA, USA), and UMass Medical School (Worcester, MA, USA).

Semen Collection and Analysis

- At age 18 years, the subjects were asked to provide two semen samples one week apart (October 2012 – February 2015).
- 133 men contributed 257 semen samples.
- Semen evaluation (SE) includes measurement of volume, sperm concentration and motility (a+b+c categories) by one technician (LS) according to the NAPA-ESHRE manual1,2.

Organochlorine Exposure Assessment

- Baseline serum samples were analyzed at the NCEH, CDC, Atlanta, USA for TCDD and 57 other organochlorine compounds (described in Burns et al).

Pubertal Measurements at Semen Evaluation

- Testicular volume was measured using the American orchidometer (which extends from 35 mL).

Statistical Analysis

Prepubertal TCDD and Semen at 18 years

- Sperm concentration, total sperm count and total motile sperm count were log transformed.
- Linear mixed models with random intercepts were used to examine the relationship between quartiles of TCDD semen concentration with semen parameters.
- Final models were adjusted for body mass index (BMI), season (spring and summer), and age.

Testicular Volume and Semen at 18 years

- Volume of left and right testicles was averaged.
- Semen parameters were log10 transformed.
- Linear univariate regression was used.

Results

Table 1. Baseline and exposure characteristics of young Russian adults

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Median (IQR or %)</th>
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</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>18.3 (18.1, 18.7)</td>
</tr>
<tr>
<td>Body Mass index, kg/m²</td>
<td>20.4 (18.8, 22.5)</td>
</tr>
<tr>
<td>Men with 2 semen samples</td>
<td>123 (63)</td>
</tr>
<tr>
<td>Abstinence time, hrs</td>
<td>70.5 (48.0, 144.0)</td>
</tr>
<tr>
<td>Serum organochlorine concentrations (µg/g lipid) TCDD</td>
<td>2.9 (1.8, 4.2)</td>
</tr>
<tr>
<td>PCDDs</td>
<td>157 (115, 200)</td>
</tr>
<tr>
<td>PCDFs</td>
<td>44.5 (29.4, 63.3)</td>
</tr>
<tr>
<td>Co-PCBs</td>
<td>198 (131, 272)</td>
</tr>
<tr>
<td>JPCBs</td>
<td>225 (152, 362)</td>
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<tr>
<td>Total TEQ</td>
<td>21.9 (16.8, 33.3)</td>
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</tbody>
</table>

Table 2. Distribution of semen parameters among 133 young Russian adults, 257 samples

<table>
<thead>
<tr>
<th>Semen parameters</th>
<th>Median (IQR)</th>
<th>WHO 2010 cut-offs</th>
<th>n (%)&lt;WHO 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm volume, mL</td>
<td>2.4 (1.8, 3.5)</td>
<td>1.5</td>
<td>48 (18%)</td>
</tr>
<tr>
<td>Sperm concentration, million/mL</td>
<td>51.3 (26.6, 78.8)</td>
<td>15</td>
<td>23 (9%)</td>
</tr>
<tr>
<td>Total sperm count, million</td>
<td>127 (61.0, 222)</td>
<td>38</td>
<td>38 (15%)</td>
</tr>
<tr>
<td>Sperm motility, %</td>
<td>64.0 (57.0, 68.0)</td>
<td>40</td>
<td>10 (4%)</td>
</tr>
<tr>
<td>Total motile sperm count, million</td>
<td>80.5 (55.8, 141)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 2. Associations between prepubertal TCDD concentration and semen parameters among 133 young Russian adults.

Figure 3. Association between average testicular volume and full total motile sperm count among young Russian adults.

Conclusion

In a prospective cohort of 18 year old Russian men:
- Higher prepubertal serum TCDD levels are associated with lower semen parameters: sperm concentration, total sperm count, and total motile sperm count.
- Higher testicular volume is associated with higher semen parameters.

In Summary

- This is one of the first prospectively designed studies to follow a large cohort of boys annually from prepuberty until young adulthood, including collection of semen samples at 18 years.
- Consistent with the Severson study, our results suggest that the prepubertal period is a sensitive window of exposure to disruptor for adult sperm quality.
- We are studying EDCs effects on sperm epigenetic programming among this Russian male cohort.

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References


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