THE IMPACT OF MATERNAL SMOKING ON OFFSPRING SEMEN QUALITY

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Smoking prevalence among women in Europe 2000-2001 (WHO 2002)

Prenatal programming and toxicity, Faroe Islands 20-24 May 2007
Trends in smoking prevalence in adult men and women in various European countries (The Tobacco Atlas by The World Health Organisation 2002)

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The chronology of earlier evidence

- Davis et al 1978 (dimethylbenzantracene in mice)
- MacKenzie and Angevine 1981 (benzo(a)pyrene in mice)
Cross section of testes of 6 week old mice exposed in-utero to benz(a)pyren 0/10/40 mg/kg oral day 2-16 of gestation (Mackenzie and Angevine. Biology of reproduction 1981: 183-191)
The chronology of earlier evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Substance/Outcome</th>
<th>Result</th>
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<tbody>
<tr>
<td>Davis et al 1978</td>
<td>dimethylbenzanthracene in mice</td>
<td>+</td>
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<td>Baird and Wilcox 1986</td>
<td>fertility in sons, DES trial</td>
<td>-</td>
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<td>Jennifer Ratcliffe et al 1992</td>
<td>semen quality, DES trial</td>
<td>-</td>
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<td>Storgaard et al 2003</td>
<td>semen in twins</td>
<td>+</td>
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<td>TK Jensen et al 2004</td>
<td>semen, military conscripts</td>
<td>+</td>
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<tr>
<td>MS Jensen et al 2005</td>
<td>semen, occupational studies</td>
<td>+</td>
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A need to

- Corroborate earlier findings in a study designed for this purpose
- Prospective collection of exposure data
Design of the most recent study

- Second generation follow-up of the ‘Healthy Habits for Two Cohort’ including 11,980 pregnant women enrolled 1984-87
- A cohort of sons were recruited to obtain a balanced distribution across maternal pregnancy smoking categories
- In all 347 sons among 716 invited were enrolled (49%)
Mobile laboratory
Total sperm count (millions) according to maternal smoking

Crude median (p75)

P=0.009

Adj mean (95% CI)

P=0.002

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Odds risk ratio for oligospermia with non-smoking as reference

![Odds risk ratio for oligospermia with non-smoking as reference](image-url)
No effect on

- morphology
- motility
- serum levels of sexual hormones
- inhibin ?
- sperm chromatin structure?
• In boys that underwent surgery for cryptorchidism, testicular biopsies revealed a severe depletion of spermatogonia and gonocytes if the mother had smoked heavily during:

  » 14% versus 37% of normal for age
Conclusion

- Fairly consistent that maternal smoking is related to a 20-40% reduction of sperm counts in the sons
- Smoking may perhaps explain part of temporal and regional shifts in sperm counts
- We know enough to warn the public, pregnant women and their spouses

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Unresolved questions

- Confounding?
- Mechanisms are largely unknown: receptor-mediated or not?
- Are epigenetic mechanisms involved?
- Thresholds?
- What about the girls?