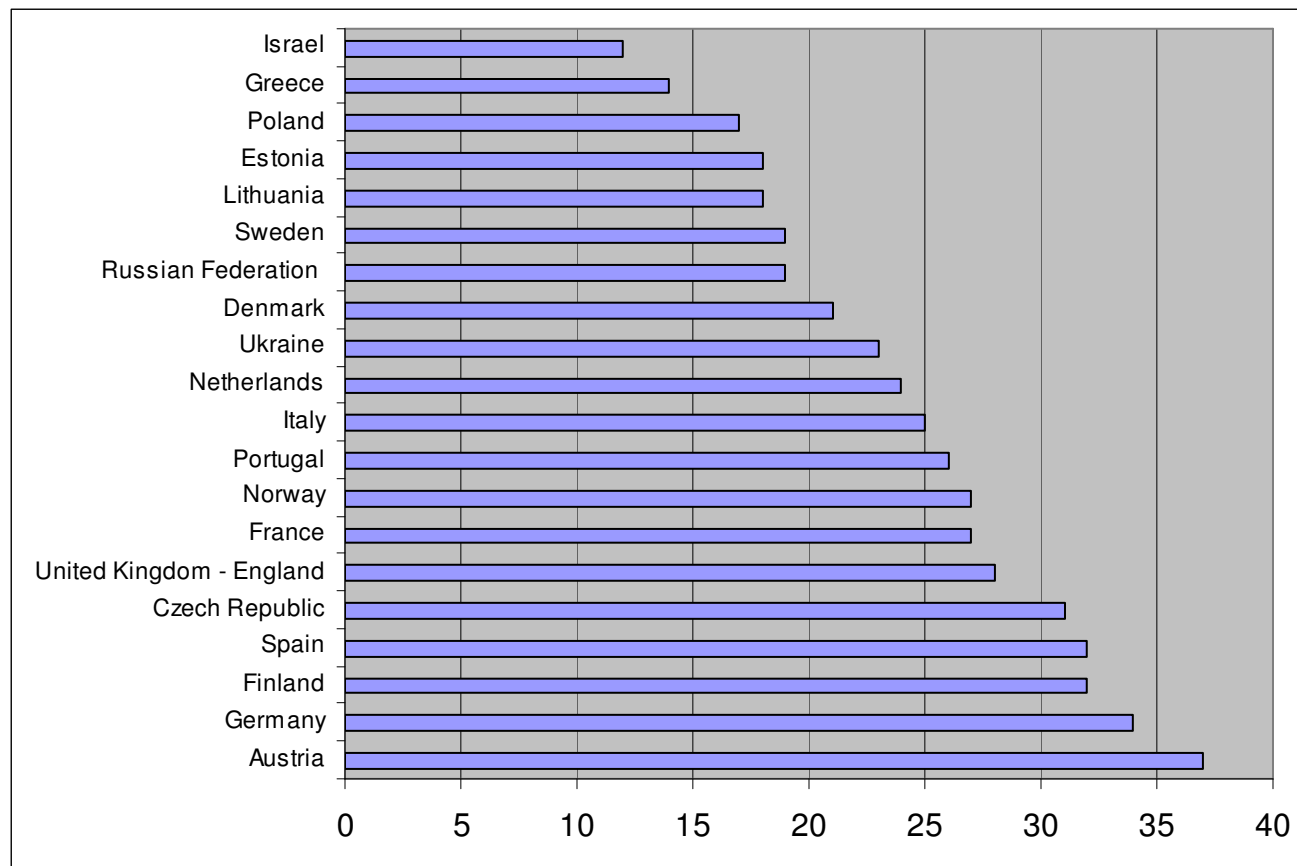




THE IMPACT OF MATERNAL SMOKING ON OFFSPRING SEMEN QUALITY

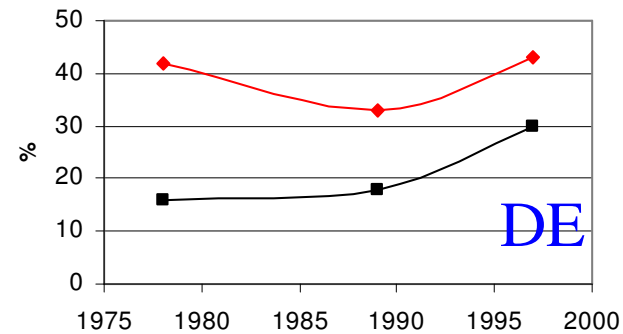
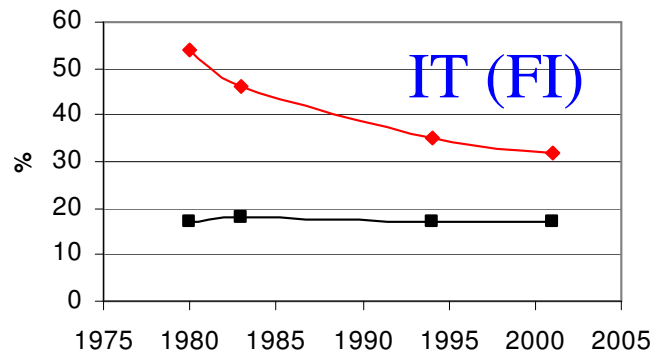
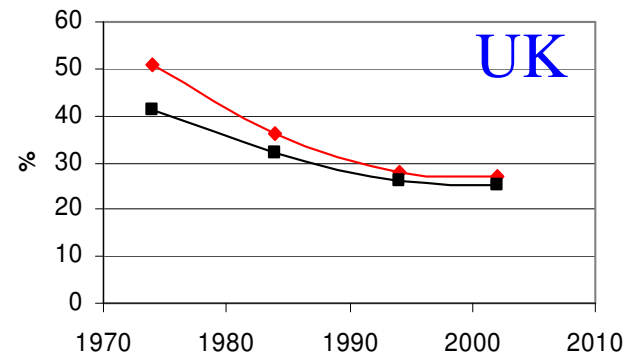
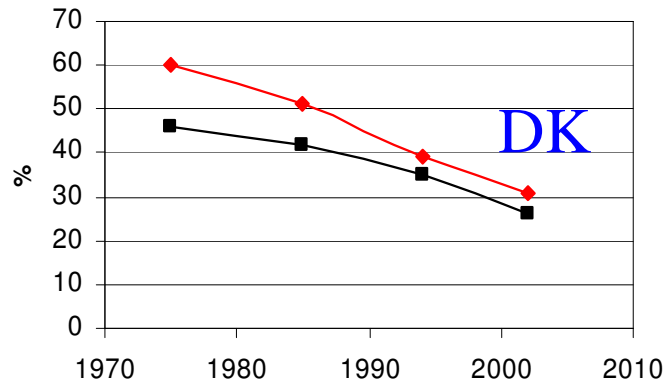
Cecilia Høst Ramlau-Hansen, Ane Marie
Thulstrup, Lone Storgaard, Gunnar Toft,
Jørn Olsen, and Jens Peter Bonde

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



Prenatal programming and toxicity, Faroe Islands 20-24 May 2007

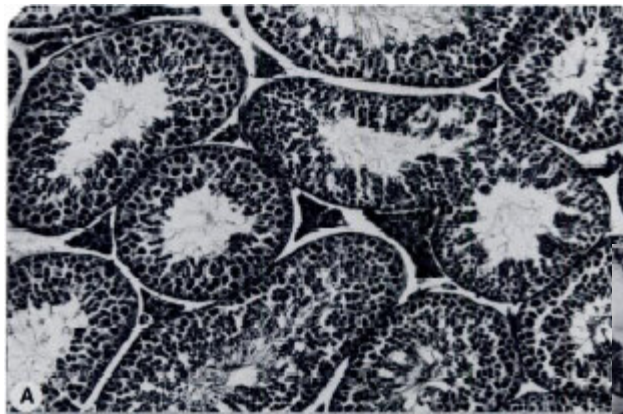
Trends in smoking prevalence in adult men and women in various European countries (The Tobacco Atlas by The World Health Organisation 2002)



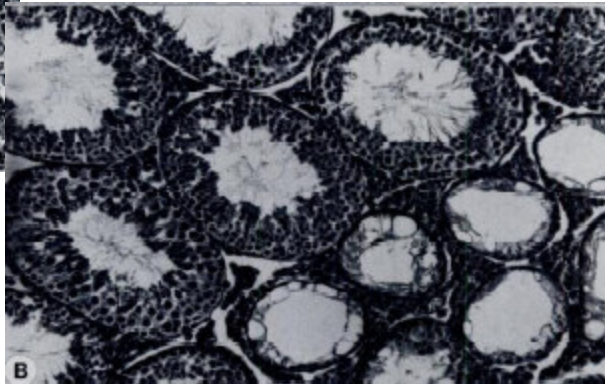
The chronology of earlier evidence

- Davis et al 1978 (dimethylbenzanthracene in mice)
- MacKenzie and Angevine 1981 (benzo(a)pyrene in mice)

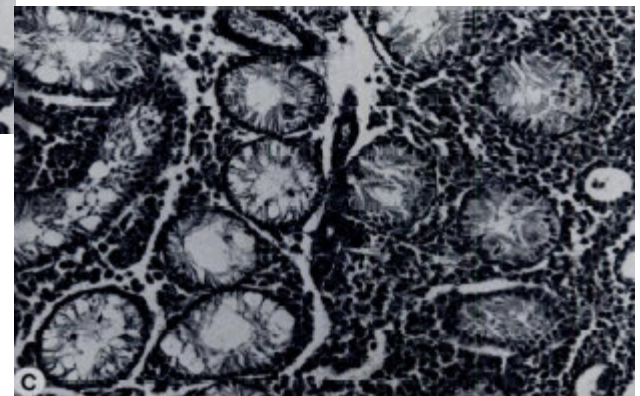
Cross section of testes of 6 week old mice exposed in-utero to benz(a)pyren 0/10/40 mg/kg oral day 2-16 of gestation (Mackenzie and Angevine. Biology of reproduction 1981: 183-191)



Reference



10 mg/kg



40 mg/kg

The chronology of earlier evidence

Davis et al 1978	dimethylbenzanthracene in mice	+
MacKenzie and Angevine 1981	benzo(a)pyrene in mice	+
Baird and Wilcox 1986	fertility in sons, DES trial	—
Jennifer Ratcliffe et al 1992	semen quality, DES trial	—
Storgaard et al 2003	semen in twins	+
TK Jensen et al 2004	semen, military conscripts	+
MS Jensen et al 2005	semen, occupational studies	+

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%)

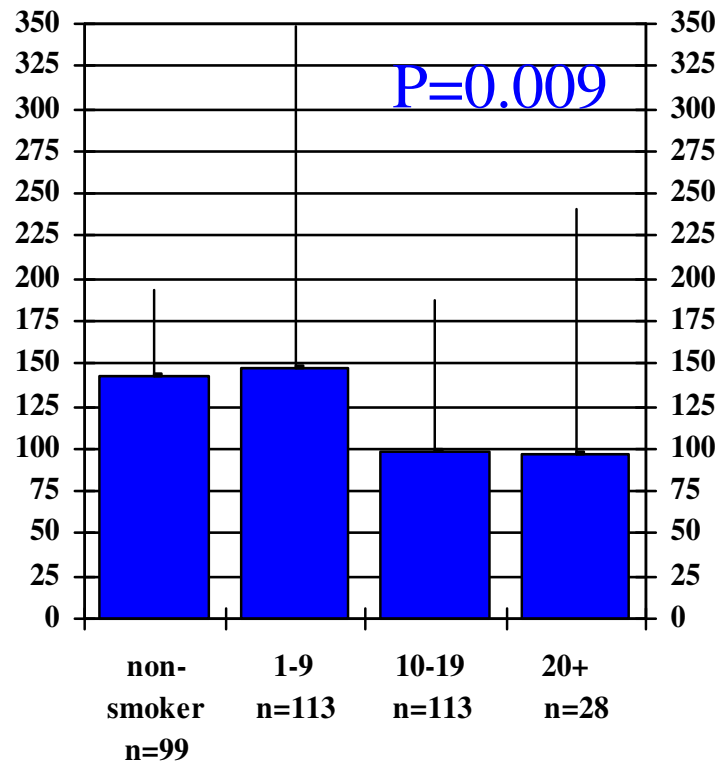
Mobile laboratory



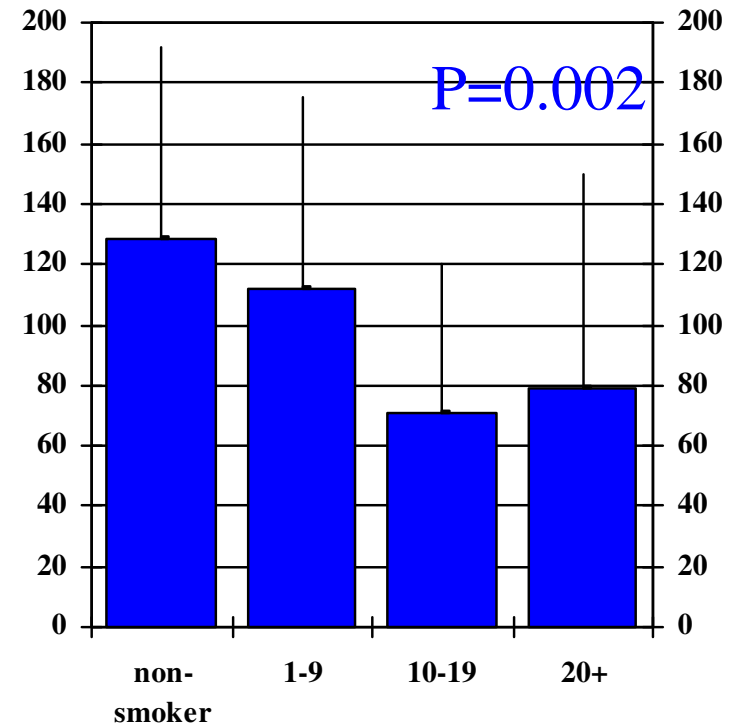
Prenatal programming and toxicity, Faroe Islands 20-24 May 2007

Total sperm count (millions) according to maternal smoking

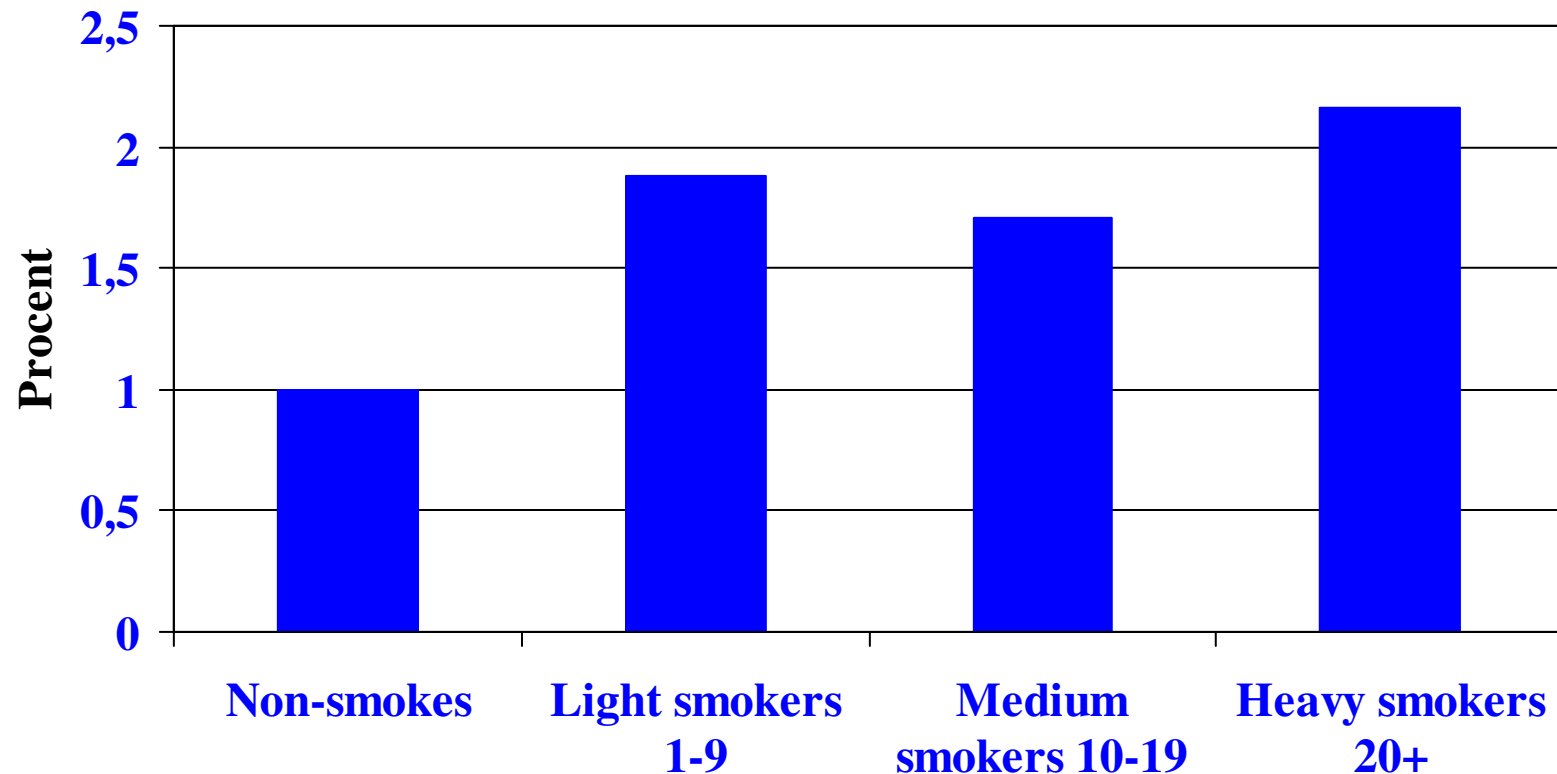
Crude median (p75)



Adj mean (95% CI)



Odds risk ratio for oligospermia with non-smoking as reference



No effect on

- morphology
- motility
- serum levels of sexual hormones

- inhibin ?
- sperm chromatin structure?

Thorup J et al. The Journal of Urology 2006: 734-37

- 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**

- **Published in American J Epidemiol March 16th 2007**

Unresolved questions

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