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Genetical and prenatal determinants for semen quality: a epidemiological twin study.

The thesis is inspired by the oestrogen hypothesis formulated by Sharpe and Skakkebaek in 1993. It put the oestrogen hypothesis to a critical test and it examines alternative determinants such as prenatal tobacco exposure and hereditary factors in male fecundity.

The thesis is based on four papers: one review of the published epidemiological literature on male reproductive disorders (low sperm count, cryptorchidism, hypospadias and testicular cancer) according to indicators of prenatal oestrogen exposure and three original articles. The aims of the thesis were 1) to put the original oestrogen hypothesis to a critical test by examining if a twin pregnancy is associated with a poor semen quality, using singleton born brothers as a reference. This study is related to the fact that oestrogen levels are much higher during a twin pregnancy than during a singleton pregnancy, 2) to study if prenatal tobacco exposure has an adverse impact on semen quality, and 3) to estimate the contribution of genetic and environment in the variation of semen quality and reproductive hormones by using the Twin method.

The study recruited monozygotic and dizygotic twins from the population based Danish Twin Registry. Randomly selected pairs of singleton brothers were retrieved from the Danish Civil Registration System. In all three groups, the men were aged between 20 to 45 years. The study population comprised of 104 monozygotic twin brothers (50 pairs), 107 dizygotic twins (51 pairs) and 105 single born brothers (51 pairs). One fresh semen sample and a blood sample were collected from all participants (316 semen samples). Information on lifestyle factors was obtained from a questionnaire filled in by the participants. Prenatal tobacco exposure was assessed from a self administrated questionnaire filled in by the mothers of the participants.

The crude and adjusted median sperm count was 19 % higher among monozygotic twins and 9 % lower among dizygotic twins in comparison with single born brothers. The findings were the opposite of what was predicted. When adjusted for potential confounders, there were no significant differences among the groups with respect to any of the measures of semen quantity and quality. These findings do not support the oestrogen hypothesis, but, on the other hand, do not reject other possible actions of environmental endocrine toxicants.

In sons of mothers, who smoked more than 10 cigarettes pr. day during pregnancy, a 47.9 % lower sperm density was found than among the unexposed (95% CI:-69.4%;-11.1%), which was consistent with a corresponding 24.2 % (95% CI:-38.2%;-7.2%) lower values of Inhibin B and 15.7 % (95% CI:-12.7%;53.5%) higher values of FSH. No effect was found for any of the other parameters. Due to the Smoking epidemic among women the findings provide a possible alternative explanation for the apparent decline in sperm counts.

By applying the twin method an estimate of the heritability of 20 % (95% CI: 0.00; 0.68) was found for sperm density. Higher hereditary factors were found for the hormones reflecting the Sertoli cell function [inhibin B: 76% (95%CI: 36; 84) and FSH:81% (95%CI: 40; 88)], for percent morphological normal cells [41% [95% CI: 0; 60]] and SCSA parameters [mean α T and COMP α T: 68% (95%CI: 34; 81) and 72% (95% CI: 25; 82) respectively].