Several reports indicate a decline in semen quality during the past decades. This suggestive evidence stems from studies of semen donors and infertile men. A meta-analysis of 61 published results of semen quality arrived at the conclusion that a genuine decline in sperm count (seminal concentration of spermatoza) took place worldwide from 1940 to 1990. However, this paper has been highly criticized for several methodological fallacies. Recent studies found no secular change in sperm count in young healthy men who volunteered in 14 medical studies or in men who banked sperm before vasectomy at three US centres over a 25-year period.

Occupational and environmental impact on male reproductive function of chemicals with hormone-like effects has received considerable interest during the past few years. One hypothesis suggests that the decline in sperm count—if real in some populations—may be caused by increasing prenatal exposure to environmental chemicals with oestrogenic effects which may cause diminished production of male fetal follicle stimulating hormone (FSH) and reduced division of Sertoli cells. Depletion of Sertoli cells is believed to be directly associated with reduced sperm output after puberty. From that point of view adult sperm count can be considered as a marker of fetal testicular development. Accordingly, examination of the relation between adult human sperm count and year of birth may provide information in support of or against the ‘prenatal’ hypothesis.

Is Semen Quality Related to the Year of Birth among Danish Infertility Clients?

YE ZHENG,* JENS PETER E BONDE,* ERIK ERNST,** JENS TØLBØLL MORTENSEN† AND JOHAN EGENSE‡


Background. There is circumstantial evidence that human sperm count may have declined during past decades. The purpose of this study was to identify the association between semen quality and year of birth.

Methods. The study comprised 8608 men consulting four Danish medical centres from 1968 to 1992 because of infertility. Data on semen quality and urogenital disorders were obtained from medical records while lifestyle data were collected from a subset of the population by a postal questionnaire (response 80%). Semen characteristics were analysed as a linear function of year of birth, centre, season and calendar year at time of semen examination, sexual abstinence and lifestyle factors. Effects of age were accounted for by restriction and stratified analysis.

Results. The sperm count declined with increasing year of birth at two of the four centres, but this association disappeared when confounders were adjusted for. Within the subset of men born 1950–1970 we revealed a decrease in the average sperm count by 1.9 mill/ml (95% confidence interval [CI] : 1.45, 2.27) per one advancing year of birth. This finding was consistent across centres even after adjustment for effects of covariates. The proportion of morphologically normal sperm cells changed in parallel with the sperm count, while semen volume did not decline in any time periods.

Conclusions. We found a birth cohort effect on sperm count and morphology among Danish infertile men born after 1950 but not in men born in the first part of the century. The findings are compatible with an environmental impact during prenatal life but the evidence is far from unequivocal.

Keywords: environment, infertility, prenatal, secular trend, semen, testis

Several reports indicate a decline in semen quality during the past decades. This suggestive evidence stems from studies of semen donors and infertile men. A meta-analysis of 61 published results of semen quality arrived at the conclusion that a genuine decline in sperm count (seminal concentration of spermatoza) took place worldwide from 1940 to 1990. However, this paper has been highly criticized for several methodological fallacies. The 61 studies were not comparable with respect to objectives, design and protocol for semen analysis, the use of linear regression was not justified by the data and the analysis did not account for possible geographical variation in sperm count. Recent studies found no secular change in sperm count in young healthy men who volunteered in 14 medical studies or in men who banked sperm before vasectomy at three US centres over a 25-year period.

Occupational and environmental impact on male reproductive function of chemicals with hormone-like effects has received considerable interest during the past few years. One hypothesis suggests that the decline in sperm count—if real in some populations—may be caused by increasing prenatal exposure to environmental chemicals with oestrogenic effects which may cause diminished production of male fetal follicle stimulating hormone (FSH) and reduced division of Sertoli cells. Depletion of Sertoli cells is believed to be directly associated with reduced sperm output after puberty. From that point of view adult sperm count can be considered as a marker of fetal testicular development. Accordingly, examination of the relation between adult human sperm count and year of birth may provide information in support of or against the ‘prenatal’ hypothesis.
The objective of this study was to examine how semen quality is related to birth year among infertile couples in Denmark. This approach is justified because a substantial secular change in the general population is expected to be paralleled by a similar trend in the semen quality of infertility clients since the sperm count distribution in fertile and infertile populations are partly overlapping (Figure 1).24

**POPULATIONS AND METHODS**

*Populations and Data Collection*

We included 8608 couples who consulted one of four Danish hospitals because of infertility. The four centres cover approximately two-thirds of the entire Danish population. Data were obtained from medical records which were available from 1981 through 1983 in Aalborg and Odense, from 1977 through 1992 in Aarhus and from 1968 through 1991 in Sønderborg. Semen analyses were performed either before or simultaneously with the examination of the female partner. In some cases each male provided several samples but only the first sample was included in this study. All centres asked for 3 days of sexual abstinence before the sample was provided, but information about the exact period of abstinence was only requested in Aarhus and Sønderborg. The samples were collected by masturbation—usually at the clinic—and were examined 1–2 hours after ejaculation. For the purposes of another study more comprehensive information was obtained in 1985 about the 3003 men who were examined between 1981 and 1983 (all centres).25 These data were partly obtained from the medical records and partly by a postal questionnaire to the male partner (response rate 80%) and included information about lifestyle habits, medical disorders, use of medicine, time taken to become pregnant (TTP) and the outcome of the female fertility examination (medical diagnosis). Table 1 gives the characteristics of the study population and Table 2 shows the distribution of potential confounding covariates on the independent variable, year of birth.

*Semen Analysis*

The seminal volume, sperm count and the percentage of morphologically normal sperm cells were determined by trained laboratory technicians at all centres. Even though the centres kept data on sperm motility we omitted this measure of semen quality because of changing methods within and between laboratories during the study period and because all manual methods which measure motility rely on subjective judgements and have poor reliability.

The semen analyses were performed as a routine investigation. In Aalborg, Odense and Sønderborg the semen volume was determined by use of a graduated cylinder with a conical base while in Aarhus the volume...
was measured by aspirating the semen sample into a graduated glass pipette. A Burger-Turk counting chamber was used to determine sperm count. The percentage of spermatooza with normal morphology were determined using stained specimens in Aalborg, Odense and Sønderborg (Odense: H-E staining; Aalborg and Sønderborg: Papanicolaou staining), while the Aarhus clinic used wet preparations viewed in a phase-contrast microscope. At all centres the cells were grouped in normal or abnormal forms until the first WHO manual
appeared in 1980. Hereafter the morphological classification was carried out according to the WHO guidelines. In this study we only examine secular trends in the proportion of abnormal sperm cells irrespective of the type of abnormal morphology. Data on variation in morphology scoring between the laboratories were not available. After reviewing the laboratory manuals we are not aware of any changes in the laboratory methods during the study period.

**Statistical Methods**

The relation between each semen characteristic and the year of birth was examined by linear regression techniques. All analyses were stratified on centre to account for the differences in sperm count and morphology across centres (Table 3). In a first step we examined the crude linear regression of the semen characteristics on birth year and if the regression coefficients did not differ across centres, we estimated the common slope using least squares regression. Secondly, we included year of semen examination (5-year intervals) and season (July–September/other months) as well as interaction terms (birth year and centre, birth year and calendar year) in multiple linear regression models to adjust for possible confounding effects. Effects of age were accounted for by the inclusion of only men aged 20–45 years, assuming that biological age has no impact on sperm count in this age range. However, in an additional series of analyses calendar time was substituted by age (dummy variables: 20–29/30–39/40–49 years) in order to adjust directly for a possible age-related effect. Adjustment for duration of sexual abstinence prior to semen sampling was undertaken in a separate analysis for the two centres providing this information (Aarhus and Sønderborg only). Finally, several other potentially confounding determinants were included in analyses confined to the subset of the samples examined between 1981 and 1983 (less than two testes [yes/no], undescended testes [yes/no], hormone treatment [yes/no], surgery on genital organs [yes/no], male urogenital diseases [yes/no], fecundity of the female partner [normal/abnormal], smoking [yes/no], alcohol consumption [≥ or <10 drinks a week]).

None of the seminal characteristics were normally distributed and the variance increased with increasing value of the parameter. The sperm count was transformed by the cubic root function to obtain equality of variance. Alternatively, we used weighted regression to account for heterogeneity of variance and to obtain directly interpretable regression coefficients. In the case of proportions—the percentage of morphologically normal sperm—logit transformation was used, while the seminal volume was normally distributed after logarithmic (base e) transformation. The goodness of fit of the regression models were evaluated by residual plots.
RESULTS

The mean sperm count declined with increasing year of birth in two of the four infertility centres (Table 3). At the Aarhus centre the mean sperm count declined by 1.4 mill/ml per year (weighted regression, 95% confidence interval [CI] : 0.1, 1.8 ) and at the Sønderborg centre by 0.9 mill/ml per year (weighted regression, 95% CI : 0.6, 1.2). However, the crude relation between sperm count and year of birth in these two centres disappeared when the calendar time of semen examination was taken into account. The sperm count decreased with advancing calendar year of examination at all centres from on average 61 mill/ml semen (95% CI : 56.1, 65.9) in 1968–1974 to 47 mill/ml (95% CI : 42.3, 51.7) in 1985–1989. The average age at the time of infertility examination increased slightly from about 30 years in 1970 to 31.5 years in 1990 (P < 0.0001) and thus men born in early years were also examined more often during the early part of the study period and vice versa. The range of birth years within 5-year windows of calendar time was fairly wide and therefore it is possible, in this rather large population, to distinguish effects of birth year from effects of calendar period when assuming that age has no effect per se within the age range 20–45 years.

We found no consistent relation between sperm count and birth year when we stratified on 5-year intervals of calendar time in a regression model which also adjusted for the effects of centre and season (Tables 3–5).

Additional regression models adjusting for effects of duration of sexual abstinence, season of sample collection, tobacco smoking and alcohol consumption produced essentially the same results. Knowledge about the fertility of the female partner was available for the 1981–1983 subset of the population. It allowed an analysis of seminal parameters in those men whose wives had reduced fecundity for one reason or another (N = 854, 9.9% of the whole population). These men may be more representative of the general population. With adjustment for centre and season, the weighted regression coefficient was –1.04 mill/ml semen per year (95% CI: –2.16, +0.88).

Semen volume did not decline with increasing year of birth in any of the four centres (Table 4). On the contrary, a highly significant increase in semen volume with increasing year of birth was found in three of the centres. Adjustment for calendar period and season resulted in a stronger relation. The adjusted mean semen volume increased from 3.38 ml in men born in 1910–1934 to 3.54 ml in men born in 1965–1975.

The time trend for the proportion of spermatozoa with normal morphology was very like the one we observed for sperm count (Table 5). At two centres the proportion of normal spermatozoa declined with increasing year of birth but this association disappeared when adjusting for effects of season and calendar period. Analyses confined to the 1981–1983 subset of

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**Table 4** Semen volume among infertility clients in four Danish centres by year of birth. Mean ± SE. Least squares linear regression coefficients

<table>
<thead>
<tr>
<th>Year of birth</th>
<th>Aalborg</th>
<th>Aarhus</th>
<th>Odense</th>
<th>Sønderborg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean SE</td>
<td>N</td>
<td>Mean SE</td>
</tr>
<tr>
<td>1925–1934</td>
<td>4</td>
<td>2.7 0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1935–1939</td>
<td>37</td>
<td>2.6* 0.3</td>
<td>5</td>
<td>2.5* 0.7</td>
</tr>
<tr>
<td>1940–1944</td>
<td>178</td>
<td>2.8* 0.1</td>
<td>61</td>
<td>3.5* 0.2</td>
</tr>
<tr>
<td>1945–1949</td>
<td>684</td>
<td>3.1 0.1</td>
<td>207</td>
<td>3.9 0.1</td>
</tr>
<tr>
<td>1950–1954</td>
<td>1155</td>
<td>3.2 0.0</td>
<td>357</td>
<td>4.1 0.1</td>
</tr>
<tr>
<td>1955–1959</td>
<td>846</td>
<td>3.3 0.1</td>
<td>273</td>
<td>4.1 0.1</td>
</tr>
<tr>
<td>1960–1964</td>
<td>405</td>
<td>3.3 0.1</td>
<td>29</td>
<td>4.3* 0.3</td>
</tr>
<tr>
<td>1965–1970</td>
<td>3319</td>
<td>3.2 0.0</td>
<td>932</td>
<td>4.0 0.1</td>
</tr>
</tbody>
</table>

Regressions

- Crude
  - Coefficient: 0.001
  - SE: 0.004

- Adjusted
  - Coefficient: 0.001
  - SE: 0.004

*
P < 0.05 by two-sided comparison with stratum 1950–1954 (unadjusted).

*Least squares linear regression of semen volume (logarithmic: base e) on birth year. Covariates included in multiple regression (adjusted values): season, calendar time of examination and abstinence period prior collection of semen sample (Aarhus and Sønderborg only).

b The linear regression coefficient differs significantly from 0 (P < 0.05).
The above results were obtained when strictly adhering to the *a priori* hypothesis that sperm count is declining steadily with advancing year of birth from 1920 to 1970. Therefore we used linear regression to analyse the data. However, the data suggest a decline in sperm count for men born in 1950 and subsequent years (Table 3). A separate analysis of the subset of men born 1950–1970 (N = 5650, 65.6% of the entire population) revealed a highly significant decrease in the average sperm count by 1.6 mill/ml (95% CI: 0.7, 2.5) per one advancing year of birth. This finding was consistent across all the four centres and robust to adjustment for confounding effects of calendar time, duration of sexual abstinence and season at sampling. Also, the sperm count declined after 1950 in each of the age strata (Figure 2). The overall centre-, season- and age-adjusted slope of sperm count on birth year was –1.86 mill/ml per year (95% CI: –1.45, –2.27). The proportion of normal sperm also declined significantly in men born after 1950 (Figure 2; *P*, 0.0001), however semen volume did not reveal any consistent changes with birth year within the subsets of the population.

**DISCUSSION**

We found no gradual deterioration in semen quality with increasing year of birth in the period 1922–1971. Although the sperm count and the proportion of sperm with normal morphology declined with increasing year of birth in two of the centres, the finding was not consistent across all centres. Furthermore, the declining trend in the two centres disappeared when adjusting for season and calendar time of semen examination. However, men born in 1950 and subsequent years had a substantial and gradual decline in sperm count and morphologically normal sperm with increasing birth year and this data driven *a posteriori* finding was robust to adjustment for potential confounders.

All studies on secular trends of semen quality (including this paper) address various highly selected populations e.g. infertile couples, semen donors, men banking sperm before vasectomy, healthy volunteers in clinical trials or men participating in occupational sperm studies. It is a matter of concern whether such groups are of any scientific value for the examination of secular changes in semen quality in the general population. While men from infertile couples are certainly not a
representative sample of the general population with respect to semen quality, the actual difference in semen profile is surprisingly small. In a study of sperm count among 1000 fertile and 800 infertile men carried out in US in 1952, the proportion of men with oligospermia was several fold higher in the infertile population giving rise to a left skewed distribution. Nevertheless, the major parts of the distributions were overlapping and the median sperm count was 90 mill/ml in fertile men compared to 69 mill/ml in infertile men (Figure 1). Therefore it is reasonable to expect that substantial changes in the sperm count distribution in the general population will be accompanied by parallel changes in the infertile population. When a female cause of infertility is identified it is less likely that reduced semen quality plays a role in the barren marriage. In our study the median sperm count was 64 mill/ml among men whose partners had a genital disorder and 42 mill/ml in the remaining group (Wilcoxon rank sum test:  \( P < 0.001 \)). In the subset of couples with female genital tract anomalies the reported associations were reproduced.

Epidemiological analyses on secular trends in semen quality are complicated by the correlation of birth year, age and time (birth year + age = calendar year) since each of the three may act as independent determinants of semen quality. This study focuses on the possible effects of prenatal exposure and for that reason we are seeking to adjust for possible effects of age and calendar year. Several cross-sectional studies have not found an age-related deterioration of sperm count between 20 and 50 years of age, but these studies are confounded if men born earlier have higher sperm counts—as hypothesized in this study. Furthermore, studies of age-related effects on sperm count may be biased if elder men with high reproductive performance are more likely to provide a semen sample. Another study of 130 men with sudden unattended death reported 30% higher daily sperm production in the younger men (N = 89, 21–50 years) than in the older men (N = 43, 51–80 years) and it has been suggested that daily sperm production peaks at 25 and decreases thereafter. Therefore we also included age in the regression models—as dummy variables to account for non-monotonous relations and as a continuous variable. This did not weaken either the strength or the significance of the decline in sperm count in men born after 1950. Furthermore, since in this cohort age is inversely related to

**Figure 2** Semen characteristics by year of birth in 8608 Danish infertility clients. Stratification on age at examination. Mean ± 2 SE.
birth year (Table 2), an effect of age would result in bias towards the null hypothesis. Sexual abstinence increases the sperm count\(^3^5\) and age might be related to sperm count because of longer duration of sexual abstinence at higher ages. However, in the Aarhus and Sønderborg population (79.7% of the entire population) there was no relation between age and abstinence period.

Age is inherently related to the time to pregnancy: the longer time a couple tries to conceive children without success, the older the couple get. If the time taken to conceive is related to sperm count, men who tried to conceive during an extended period of time would for that reason be older but also have reduced sperm count—thus creating selection bias towards null. In our population, older people had a longer TTP in their most recent pregnancy (age 20–30 years: mean TTP 30 months, SE = 19.2; age 30–45 years mean TTP 40 months, SE = 31.1; \(P < 0.001\)), but the TTP was not related to sperm count (TTP <24 months: mean sperm count = 70 mill/ml, SE = 81.05; TTP ≥24 months: mean sperm count = 70 mill/ml, SE = 74.69; \(P > 0.05\)). Therefore, the longer TTP in older men may rather be caused by reduced fecundity of the spouse.

Calendar year may be related to semen quality in this sample of infertile men through several mechanisms. Obviously laboratory methods may change over time within a laboratory. It seems, however, that the minor differences in the laboratory methods used at the four laboratories cannot account for the changes in semen parameters seen during the period. Urogenital infections, lifestyle, clothing, occupational and environmental exposures, sexual habits and attitudes towards family size are other factors which may change with calendar time and have direct or indirect impact on male reproductive function. Yet another mechanism by which calendar time may confound the relation between semen quality and birth year is via time dependent change of the proportion of men seeking medical examination for infertility. A Danish survey from the early 1980s indicated that only one-third of infertile couples is referred to hospital.\(^3^6\) Accordingly, bias because of time dependent change in the pattern of seeking medical examination among infertile couples or time dependent change in risk factors for adult reproductive function cannot be ruled out. Therefore adjustment for calendar time is crucial and in this study the apparent effect of birth year on sperm count in two centres disappeared when adjusting for calendar time.

The proportion of men with azoospermia was almost constant across birth years and calendar time (Table 2; logistic regression of azoospermia on year of examination: OR = 1.007, 95% CI: 0.99, 1.02). This is taken as evidence that a possibly increased awareness of options for infertility treatment has not made it more likely for more severely infertile men to attend examination in later years.

Our finding that the sperm count declined from an average 61 mill/ml (95% CI: 56.1, 65.9) in 1968–1974 to 47 mill/ml (95% CI: 42.3, 51.7) in 1985–1989 is in agreement with the findings among fertile Parisian semen donors (decline from 89 mill/ml in 1973 to 60 mill/ml in 1992); among Scottish semen donors (decline from 98 mill/ml among donors born before 1959 to 78 mill/ml among donors born after 1970) and with a study of Danish infertility clients which reported a decline in sperm count from 90 mill/ml in 1952 to 65 mill/ml in 1972.\(^7\) None of these studies reported calendar time adjusted estimates of the relation between sperm count and birth year. However, our study does not corroborate the results of a meta-analysis comparing published sperm densities in men with proven or unknown fertility.\(^1^0\) This meta-analysis did not reveal reduced sperm counts in men examined in 1960 and subsequent years, but this study is biased due to incomparability of the various populations.

In conclusion, semen quantity and quality among Danish infertility clients has not deteriorated steadily with increasing year of birth during the entire period from 1922 to 1972. However, from 1950 onwards there was a gradual decline in sperm count and normal sperm forms but not in semen volume. This is far from unequivocal evidence that the sperm count in the general male Danish population has changed during past years. So far several pieces of the puzzle are still missing and there is an obvious need to examine other data as well.

ACKNOWLEDGEMENTS

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REFERENCES


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