Evidence of deteriorating semen quality in the United Kingdom: birth cohort study in 577 men in Scotland over 11 years

Stewart Irvine, Elizabeth Cawood, David Richardson, Eileen MacDonald, John Aitken

See editorial, pp471, 506

Abstract

***Objective*—To determine whether the quality of semen has changed in a group of over 500 Scottish men born between 1951 and 1973.**

***Design*—Retrospective review of data on semen quality collected in a single laboratory over 11 years and according to World Health Organisation guidelines.**

***Setting*—Programme of gamete biology research funded by Medical Research Council.**

***Subjects*—577 volunteer semen donors. Of these, 171 were born before 1959, 120 were born in 1960-4, 171 in 1965-9, and 115 in 1970-4.**

***Main outcome measures*—Conventional criteria of semen quality including semen volume (ml), sperm concentration (10^6/ml), overall motility (% motile), total number of sperm in the ejaculate (10^6), and total number of motile sperm in the ejaculate (10^6).**

***Results*—When the four birth cohort groups were compared a later year of birth was associated with a lower sperm concentration, a lower total number of sperm in the ejaculate, and a lower number of motile sperm in the ejaculate. The median sperm concentration fell from 98×10^6/ml among donors born before 1959 to 78×10^6/ml among donors born after 1970 ($P=0\cdot002$). The total number of sperm in the ejaculate fell from 301×10^6 to 214×10^6 ($P=0\cdot0005$), and the total number of motile sperm in the ejaculate fell from $169\cdot7\times10^6$ to $129\cdot0\times10^6$ ($P=0\cdot0065$).**

***Conclusion*—This study provides direct evidence that semen quality is deteriorating, with a later year of birth being significantly associated with a reduced number of sperm in adult life.**

Introduction

Although the meta-analysis by Carlsen *et al* attracted much attention,[1] the suggestion that the quality of human semen may be deteriorating is not new.[2-7] Examining data on 14 947 men that had been published in 61 papers between 1938 and 1991, Carlsen *et al* observed a clearly significant decline in average sperm concentration ($0\cdot94\times10^6$/ml/year) corresponding to a decline from 113×10^6/ml in 1940 to 66×10^6/ml in 1990. Furthermore, they drew attention to the fact that this change was happening in association with an increase in the reported incidence of congenital malformations of the male genital tract, such as cryptorchidism[8] and hypospadias,[9,10] and a striking increase in the rates of registration of testicular cancer.[11,12] These developments led Sharpe and Skakkebæk to postulate that the observed changes may have a common origin in perinatal life, perhaps mediated through exposure to environmental xenoestrogens.[13] More recently, Auger *et al* reported a decline in the semen quality of a large group of French men, noting that both older age (at ejaculation) and a later year of birth were associated with a decline in the conventional criteria of semen quality.[14]

The meta-analysis of Carlsen *et al* has been criticised because the studies included were undertaken in different countries and at different times and therefore bias in subject recruitment or changes in methods of semen analysis may have affected the results.[15] In a similar way, the study by Auger *et al* was criticised for selection bias (only men of proved fertility were studied) and because only one semen sample from each man was included.[16] Although there is, as yet, no clear evidence that male fertility, as opposed to semen quality, is declining, the issue of whether later birth cohorts have poorer quality semen is important.[17,18] We examined semen quality in a large group of unselected men contributing semen samples to a programme of gamete biology research in the United Kingdom.

Subjects and methods

Subjects were volunteer donors who had offered to provide semen samples for this unit's programme of gamete biology research. Recruitment was by several approaches, including discussions at antenatal parent craft groups, advertisements to undergraduate populations, and personal contact by existing donors. Each potential donor was seen and counselled by the research support and clinical staff of the programme. All participants gave written informed consent to the use of their semen for research according to local guidelines, which incorporated those promulgated by the British Andrology Society[19] and the Human Fertilisation and Embryology Authority.

Before the submission of their first sample donors were not selected on the basis of proved fertility or the absence of factors associated with impaired quality of semen. This study is based on a cohort of 577 donors who joined the programme between 1984 and 1995. The donor's date of birth, date of submission of first sample, and results of semen analysis were recorded. The median age of this group of donors at the time of providing their first sample was 27 (10th-90th centile 20-36). Over a quarter (144) were professional men (social classes I and II), 14·3% (82) were in social class IIIN (non-manual), 14·1% (81) were in manual occupations, and only 5·2% (30) were unemployed. Information on occupation was unavailable for 16 (2·8%) subjects. Less than 40% (224) were students and almost half (43·5%, 251) were of proved fertility.[20] Information on fertility was unavailable for 11 (1·99%) subjects.

ANALYSIS OF SEMEN

All semen samples were analysed in one laboratory according to a standardised method. The normal reference range was that defined for our local population (sperm concentration $\geq20\times10^6$/ml and overall motility $\geq40\%$)[21] and remained unchanged throughout the period of the study.[15] The first sample submitted by each volunteer was analysed, and donors

Medical Research Council Reproductive Biology Unit, Centre for Reproductive Biology, Edinburgh EH3 9EW
Stewart Irvine, *consultant*
Elizabeth Cawood, *scientific officer*
David Richardson, *research officer*
John Aitken, *professor*

Reproductive Medicine Laboratories, University of Edinburgh, Centre for Reproductive Biology, Edinburgh EH3 9EW
Eileen MacDonald, *medical laboratory scientific officer*

Correspondence and requests for reprints to: Dr Irvine.

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Table 1—*Quality of semen of 577 volunteer semen donors. Values are means (SD) unless stated otherwise*

	All donors	Birth cohorts			
		≤1959	1960-4	1965-9	1970-4
No of donors	577	171	120	171	115
Age at donation (years):					
Mean (SD)	27·0 (6·4)	34·4 (4·4)	28·5 (3·2)	23·1 (3·0)	20·3 (1·6)
Range	18-53	27-53	20-35	19-30	18-25
No (%) known to be fertile*	251 (44)	138 (81)	78 (65)	29 (17)	6 (5)
Quality of semen:					
Ejaculate volume (ml)	3·4 (1·7)	3·6 (1·7)	3·3 (1·6)	3·6 (1·7)	3·0 (1·6)
Sperm concentration ($\times 10^6$/ml)	104·5 (80·2)	117·9 (88·6)	114·4 (84·4)	91·3 (75·8)	93·9 (63·9)
Overall motility (%)	61·3 (14·4)	59·8 (13·0)	61·4 (13·9)	62·1 (13·5)	62·4 (18·1)
Total No of sperm in ejaculate ($\times 10^6$)	345·2 (339·4)	431·7 (474·6)	353·5 (267·2)	308·1 (266·3)	262·8 (213·6)
Total No of motile sperm in ejaculate ($\times 10^6$)	211·6 (204·2)	254·5 (274·9)	219·0 (169·8)	191·7 (159·5)	169·7 (156·8)

*Information unavailable for 16 subjects.

Table 2—*Relations between measures of semen quality and year of donor's birth and age at donation (linear regression analysis)*

	Regression coefficient (95% confidence interval) (percentage change)	P value
Later birth (by 1 year)		
Ejaculate volume (ml)	−0·01 (−0·03 to 0·01)	>0·05
Sperm concentration ($\times 10^6$/ml)	−2·1 (−1·92 to −2·42)*	0·002
Total No of sperm in ejaculate ($\times 10^6$)	−2·01 (−1·84 to −2·30)*	0·0001
Overall motility (%)	0·18 (0·02 to 0·34)	0·0322
Total No of motile sperm in ejaculate ($\times 10^6$)	−2·04 (−1·85 to −2·40)*	0·0005
Older age (by 1 year)		
Ejaculate volume (ml)	0·01 (−0·01 to 0·03)	>0·05
Sperm concentration ($\times 10^6$/ml)	2·07 (2·41 to 1·89)*	0·0003
Total No of sperm in ejaculate ($\times 10^6$)	2·04 (2·36 to 1·83)*	0·0003
Overall motility (%)	0·06 (−0·12 to 0·24)	>0·05
Total No of motile sperm in ejaculate ($\times 10^6$)	4·27 (1·71 to 6·82)*	0·0011

*Back transformed from the regression coefficient of the log transformed variable.

were instructed to abstain from ejaculation for three or four days before giving it. Samples were collected by masturbation into sterile plastic containers.

The sample was allowed to liquefy at 37°C for 30 minutes before analysis, which was within 90 minutes of ejaculation. In general, samples were analysed according to the guidelines of the World Health Organisation.[22-24] The volume of the ejaculate (ml) was determined by aspirating the liquefied sample into a graduated disposable pipette. To determine the concentration of sperm (10^6/ml), 10 μl of gently mixed semen was thoroughly mixed with 190 μl of sperm diluting fluid (50 g sodium bicarbonate in 10 ml of 35% formaldehyde per litre of water and loaded in duplicate into the chambers of a haemocytometer (Improved Neubauer, BDH, Lutterworth, Leicestershire). The haemocytometer was examined under a microscope (Ortholux, Leitz, Wetzlar, Germany) at a final magnification of 400 times, and the mean of the counts obtained in the two chambers was calculated. Motility was examined by placing a 20 μl drop of mixed semen on to a prewarmed microscope slide, which was covered with a coverslip (19×19 mm). This preparation was examined at a magnification of 400 times under phase contrast illumination; with the aid of an eyepiece graticule the slide was scanned and at least 100 sperm were examined in four to six randomly chosen fields.

Overall motility was determined as the proportion of sperm showing evidence of movement (WHO grades a, b, and c) to the total number of spermatozoa counted (WHO grades a, b, c, and d).[24] The percentage of morphologically normal sperm was not routinely determined in the first samples from this group of donors.

STATISTICAL ANALYSIS

Data were collected in standard microcomputer spreadsheets and analysed using both SPSS version 6.0 for Windows (SPSS, Chicago, Illinois, USA) or STATISTICA-MAC version 4.1 (Statsoft, Tulsa, Oklahoma, USA). The distribution of variables was examined and when appropriate, variables were normalised before analysis by log transformation. Ejaculate volume, sperm concentration, and the derived variables of total number of sperm in the ejaculate (ejaculate volume×sperm concentration;× 10^6 sperm) and total number of motile sperm in the ejaculate (ejaculate volume×sperm concentration× motility/100;× 10^6 sperm) were not normally distributed.

In general, data are presented as medians (10th-90th centile), except when indicated otherwise. Relations between variables were examined using linear and stepwise multiple linear regression. In addition, donors were divided into four roughly equal cohorts of five years according to year of birth: 1955-9, 1960-4, 1965-9, and 1970-4. For the purposes of this analysis, the 65 (11·3%) donors born before 1955 were included in the first birth cohort. Differences between groups were examined by analysis of variance or Kruskal-Wallis analysis of variance with comparison of medians as appropriate.

Results

When the age of donors was examined with respect to the year of their first donation, there was no evidence that the age of donors had changed during the period of data collection. Table 1 shows the age, fertility, and semen quality of the study population. As expected, few men in the younger birth cohorts were of proved fertility.

When semen quality was examined in relation to donors' year of birth, several significant negative relations were observed, suggesting that donors born later tended to have poorer quality semen. Ejaculate volume did not correlate with either year of birth or age at donation. In contrast, sperm concentration decreased by 2·1% per year, the total number of sperm in the ejaculate by 2·01%, and the total number of motile sperm in the ejaculate by 2·04% per year (table 2). Overall motility was weakly positively related to a later year of birth, increasing by 0·18% per year. Because the donors born earlier are older, similar relations but with opposite sign were observed between age at donation and semen quality (table 2) There were no relations between the year of donation and any measures of semen quality, with the exception of overall motility, which increased by 1·2% per year (95% confidence interval 0·87 to 1·62, $P<0·0001$).

Because the process of aging is associated with a

Table 3—*Median values (with 10th-90th centiles) for measures of sperm quality in 577 volunteer semen donors*

	All donors (n=577)	Birth cohort ≤1959 (n=171)	1960-4 (n=120)	1965-9 (n=171)	1970-4 (n=115)	P value*
Sperm concentration ($\times 10^6$/ml)	86·0 (26·0-196·8)	98·0 (38·6-218·4)	91·7 (34·0-205·8)	75·5 (22·1-170·4)	78·0 (21·0-166·4)	0·002
Total No of sperm in ejaculate ($\times 10^6$)	262·5 (77·9-680·3)	301·0 (101·6-706·8)	297·4 (76·2-634·6)	235·0 (71·2-516·4)	214·0 (54·0-526·5)	0·0005
Overall motility (%)	62·0 (43·0-79·0)	61·0 (41·6-76·0)	63·0 (44·0-78·0)	62·0 (44·0-80·0)	64·0 (38·1-83·9)	>0·05
Total No of motile sperm in ejaculate ($\times 10^6$)	155·0 (43·5-434·0)	169·7 (52·3-503·9)	179·4 (46·2-436·4)	143·6 (43·6-410·3)	129·0 (29·0-325·8)	0·0065

*Comparison among birth cohors by Kruskal-Wallis test.

deterioration in semen quality,[25] a series of stepwise multiple linear regression analyses was undertaken in which both age at donation and year of birth were entered against the various measures of semen quality. On each occasion only one variable, usually year of birth, was selected and was negatively related to semen quality. In the case of the total number of motile sperm in the ejaculate, age at donation was selected because of its stronger positive relation with this variable. In other words, it was not possible in this dataset to observe a negative relation between age and semen quality that was independent of year of birth.

Table 3 and figures 1 and 2 show the semen quality of the four birth cohorts. The median sperm concentration ($\times 10^6$/ml) among donors born in the 1950s was 98·0 (10th-90th centile 38·6-218·4), falling to 78·0 (21·0-166·4) among those born in the 1970s (P=0·002) (fig 1). The overall percentage of motile sperm did not show any change from the 1950s cohort to the 1970s cohort (61·0 (41·6-76) *v* 64·0 (38·1-83·9); fig 1), but the total number of motile sperm in the ejaculate ($\times 10^6$) fell from 169·7 (52·3-503·9) to 129·0 (29·0-325·8), a fall of almost 24% (fig 2). Similar results were observed when the log transformed variables were examined by analysis of variance (figs 1 and 2).

Discussion

So far as we know, these data are the first evidence that the quality of semen is deteriorating in the United Kingdom. Our findings support previous reports that the quality of human semen seems to be falling.[1,14] In particular, we have observed a decline in sperm concentration and the total number of sperm and of motile sperm in the ejaculate in association with a later year of birth, such that men born in the 1970s are producing some 24% fewer motile sperm in their ejaculate than are men born in the 1950s. Auger *et al* observed that the decline in sperm concentration was some 2.6% per annum with later year of birth,[14] while we found that this figure was 2·1%. Unlike Auger *et al*, we could not show the independent effect of older age on semen quality, reflecting the larger number of subjects, greater age range, and longer data collection period in their study.

As the within subject coefficient of variation for the conventional criteria of semen quality is high,[16] it has been suggested that it may be more valid to use multiple semen samples from each donor. In this study we included only the first sample provided by each volunteer to minimise the effects of selection bias resulting from the later exclusion of donors with subnormal semen quality.[15] Although we did not record the duration of abstinence separately, all donors were asked to abstain for three to four days before giving their first sample. The duration of abstinence affects several measures of semen quality, most notably ejaculate volume,[26] and younger donors would be expected to have shorter periods of abstinence, confounding the assessment of semen quality. However, no association was seen between either age (at ejaculation) or year of birth and ejaculate volume.

STUDY POPULATIONS

Previous studies addressing the issue of secular changes in semen quality have tended to concentrate on selected groups of men, which has raised concern about the possible influence of selection bias. For example, Nelson and Bunge reported data on patients presenting for vasectomy.[2] These men had an average sperm concentration of 48×10^6/ml, with 20% being below 20×10^6/ml and 7% above 100×10^6/ml.[2] They contrasted these observations with those of MacLeod and Gold in a group of 1000 men of proved fertility; these men had an average sperm concentration of 107×10^6/ml, only 5% being below 20×10^6/ml and 38% above 100×10^6/ml.[27]

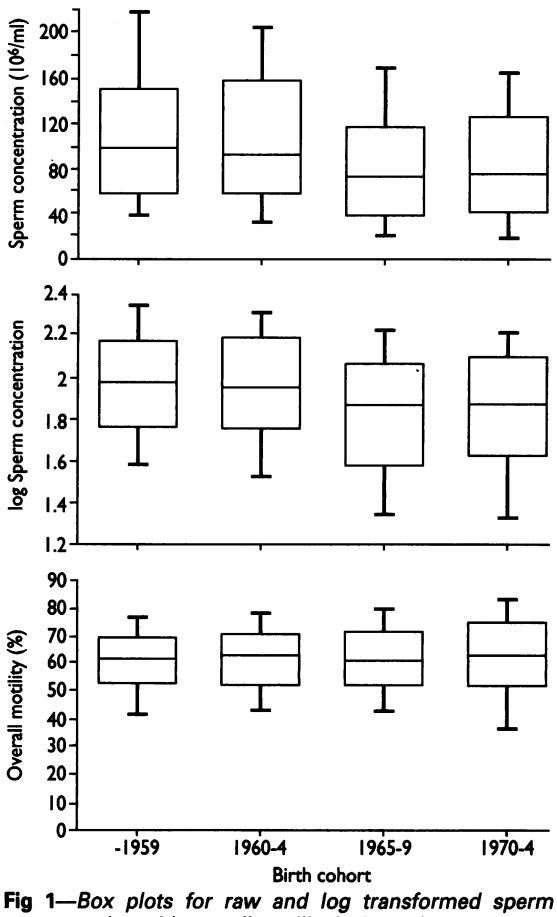

Fig 1—*Box plots for raw and log transformed sperm concentration with overall motility in 577 volunteer semen donors according to birth cohort. Changes in sperm concentration were significant (P=0·002) by Kruskal-Wallis test, changes in overall motility were not*

Data have also been collected on men donating semen for therapeutic donor insemination. For example, Leto and Frensilli reported data on 275 such donors and noted that the average sperm concentration (a mean of 12 replicates for each man) fell from 120×10^6/ml in 1973 to almost 90×10^6/ml in 1980.[4] Most commonly studied, and most subject to changing selection bias, are the male partners of couples presenting with infertility. MacLeod and Wang, for example, reported data on the male partners of 1300 infertile partnerships and saw no appreciable secular trend over three decades.[28] However, Bostofte *et al* noted a fall in the median sperm concentration from $73{\cdot}4\times10^6$/ml to $54{\cdot}5\times10^6$/ml when they compared the semen quality of 1077 Danish men examined in 1952 with that of 1000 similar men examined in 1972.[5] In a similar study in Sweden Osser *et al* compared 185 men in 1980-1 with a similar number of age matched controls from 1960-1.[7] They observed that the mean sperm concentration fell from $125{\cdot}4\times10^6$/ml in 1960 to 78×10^6/ml in 1980.

OESTROGEN HYPOTHESIS

We emphasise that there is, as yet, no evidence that male fertility, as opposed to semen quality, is declining. Not only are the conventional criteria of semen quality poor indicators of fertility[29 30] but it is difficult to judge from the available epidemiological evidence whether the prevalence of infertility is changing.[31] Our data indicate that a later year of birth is associated with poorer semen quality in adult life. As such, it is consistent with the hypothesis advanced by Sharpe and Skakkebæk that environmental or other factors acting during fetal and perinatal life can have profound effects on subsequent adult reproductive function,[13] but it would also be consistent with environmental factors acting much later in life. A recent report has drawn attention to the possibility that xenoestrogens may be implicated,[18] and data from experiments in animals support the hypothesis that perinatal exposure to known environmental xenoestrogens results in alterations in testicular size and sperm production in adulthood.[32] Urgent research is required to measure these apparent changes in human semen quality more widely, to examine apparent regional variations, to examine sperm function as opposed to simply sperm number, and to assess whether such changes are having any impact on human health and male fertility.

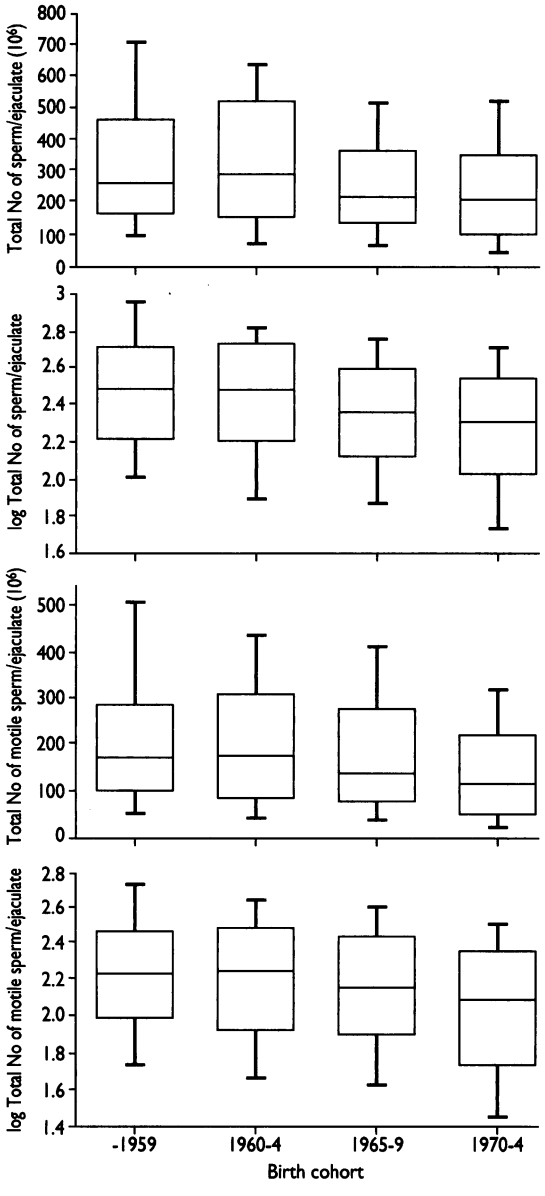

Fig 2—*Box plots for raw and log transformed total sperm counts in ejaculate and for total number of motile sperm in ejaculate in 577 volunteer semen donors according to birth cohort. Changes in total number of sperm and total number of motile sperm were significant (P=0·0005 and P=0·0065 respectively) by Kruskal-Wallis test*

Key messages

- This study provides the first evidence that the quality of human semen is deteriorating in the United Kingdom
- When men born in the 1970s were compared with men born in the 1950s, the total number of motile sperm in the ejaculate was reduced by almost 25%
- These data confirm previously published data from other countries that semen quality is changing, declining by about 2·1% per year
- Research is urgently required to examine the function as well as the number of sperm and to assess whether these changes are affecting human health and male fertility

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Conflict of interest: None.

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Time series analysis of sperm concentration in fertile men in Toulouse, France between 1977 and 1992

L Bujan, A Mansat, F Pontonnier, R Mieusset

See editorial, pp 467, 506

Abstract

***Objectives*—To investigate whether sperm production has changed during the past 16 years in the Toulouse area of France.**

***Design*—Time series analysis of sperm donors' specimens between 1977 and 1992.**

***Setting*—Sperm bank of university hospital in Toulouse, France.**

***Subjects*—302 healthy fertile men candidate sperm donors more than 20 and up to 45 years old and without any infertile brothers.**

***Main outcome measure*—Spermatozoa concentration.**

***Results*—Donors' mean age at time of donation was 34·05 (SD 5·13), but this increased significantly ($P<0·001$) during the study, from 32·4 in 1977 to 36 in 1992. Mean sperm count of samples was $83·12\times10^6$/ml (SD $68·42\times10^6$/ml). Sperm concentration was positively linked to the year of donation (Pearson's coefficient $r=0·12$, $P<0·05$), but this correlation disappeared after adjustment for age of donors ($r=0·09$, $P>0.05$).**

***Conclusion*—Sperm concentration has not changed with time in the Toulouse area.**

Table 1—*Age of sperm donors by year when sample donated*

Year	No of donors	Age (years) Mean	Range
1977	11	32·4	25-42
1978	22	32·2	21-43
1979	27	31·7	24-39
1980	23	31·4	22-44
1981	25	33·4	26-41
1982	27	32·3	24-44
1983	15	35·7	28-43
1984	26	36·5	26-44
1985	17	35·2	27-41
1986	17	37·2	30-44
1987	14	35·2	21-44
1988	14	34·6	27-39
1989	21	34·4	27-43
1990	17	35·5	27-44
1991	15	34·5	25-43
1992	11	36·0	30-43

CECOS Midi-Pyrénées and Centre de Stérilité Masculine, Centre Hospitalier Universitaire La Grave, 31052 Toulouse, France
L Bujan, *associate professor of reproductive biology*
A Mansat, *associate professor of reproductive biology*
F Pontonnier, *professor of urology*
R Mieusset, *associate professor of histology*

Correspondence to:
Dr Bujan.

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Introduction

Several studies have suggested that the sperm count of healthy men has declined in the past few decades. Carlsen *et al* recently reported a decrease in sperm count and volume in the past 50 years.[1] This decrease was confirmed by Auger *et al* in the Paris area of France and was associated with qualitative alterations of sperm—that is, decreased motility of spermatozoa and fewer normally shaped spermatozoa.[2] Moreover, other studies have reported increases in the incidence of cryptorchidism[3] and testicular cancer.[4,5]

Several hypotheses have been suggested to explain this decrease in sperm quality—for example, environmental exposure to harmful compounds[6] such as oestrogens or compounds with oestrogen-like activity.[7] In order to investigate potential environmental factors, we analysed the quality of semen supplied by donors to our sperm bank in south west France, a less populated area than Paris and one with different water supplies and air quality.

Methods

We studied the first ejaculates from healthy unpaid candidate sperm donors that were collected between 1977 and 1992 in our centre (Centre d'Etude et de Conservation des Oeufs et du Sperme Humain Midi-Pyrénées). All the donors had previously fathered at least one child. We excluded donors aged less than 20 and over 45 as age can affect the characteristics of sperm[8] and excluded donors with an infertile brother.[2]

Donors provided semen samples by masturbation at the laboratory after a recommended period of sexual abstinence of three to five days. The samples were analysed as described previously.[9] Sperm counts underwent logarithmic (base 10) transformation before statistical analysis, which was done with the PCSM package (Delta Soft, Meylan, France).

Results

We included 302 candidate donors in the study: 113 lived in the Toulouse conurbation, 64 lived in smaller cities, 115 lived in small towns or rural areas, and 10 came from other parts of France. The donors' mean age at the time of donation was 34·05 (SD 5·13, range 21-44), but this increased significantly ($P<0·001$) during the study from 32·4 in 1977 to 36 in 1992 (table 1).

The mean sperm count of the samples was $83·12\times10^6$/ml (SD $68·42\times10^6$/ml). Figure 1 shows the sperm counts according to the year of donation. Linear regression analysis between sperm count and year of donation showed a positive relation (Pearson's coefficient $r=0·12$, $P<0·05$). However, when adjustment was made for the donor's age the relation between sperm count and year of donation was no longer sig-

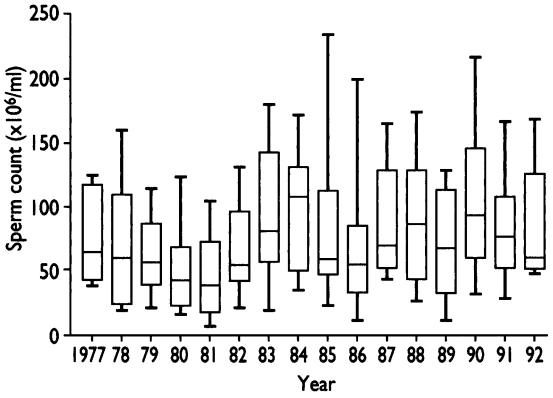

Fig 1—*Sperm count of semen samples by year when sample donated (box plots represent median and first and third quartile; bars represent 10th and 90th centiles)*