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OPINION

Trends in global semen parameter values

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Allegations for a worldwide decline in semen parameter values have not withstood scientific scrutiny. Methodological flaws in an influential 1992 paper are summarized here, and studies that have been published since 1992 are reviewed. Of the 35 major studies of time trends in semen quality reviewed here, eight (a total of 18 109 men) suggest a decline in semen quality; 21 (112 386 men) show either no change or an increase in semen quality; and six (26 007 men) show ambiguous or conflicting results. The cause (or causes) of the geographical and temporal variations in semen parameter values reported by these diverse studies deserve further investigation.

This paper critically examines two related scientific assertions: that there have been worldwide declines in semen quality in recent decades and that these declines are related to environmental exposure to minute levels of 'endocrine disruptors' (chemicals that exhibit some degree of estrogen-like activity in the body). The data supporting these assertions will be demonstrated to be weak, at best. Reported declines in semen parameter values are likely to be either highly local phenomena with an unknown etiology or the result of methodological errors arising from attempts to observe highly variable physical attributes (semen characteristics) with relatively low-resolution tools (retrospective analysis of nonrandomized study populations).

METHODOLOGICAL CHALLENGES

For many reasons, semen may be the most poorly understood bodily fluid, in terms of the distribution of its normal values in the general population. One problem is the relative difficulty of obtaining human semen for scientific analysis. The fact that semen is most readily obtained by masturbation poses significant logistical barriers to objective, randomized, longitudinal studies of semen parameters in community-dwelling men. For example, participation rates in the few studies that have attempted to assess semen quality in non-infertile men have typically been <20%).[1,2] Although it is possible, in principle, to conduct large-scale population-based trials, the procedural issues involved are challenging, which is likely the reason that such trials have not yet been conducted. Instead, research to date on semen quality has relied on populations of men who have provided semen samples for sperm donation, infertility evaluation, prevasectomy evaluation, or for other specific reasons. Each of these populations presents a possible selection bias and none represent a random sample of the population at large. For example, semen donors may have been screened for problems known to affect fertility, or they may have been selected precisely because a prior semen analysis indicated robust fertility. Male donors in cases of *in vitro* fertilization or other attempts to overcome infertility issues, on the other hand, are more likely to have low fertility, regardless of the fertility status of their partner. It is, therefore, fundamentally difficult at present to determine 'normal' semen parameters for community-dwelling populations of men.

In addition, semen attributes such as sperm count, semen volume and sperm morphology vary widely between individuals as well as within individuals over time. Longer periods of time since the previous ejaculation (abstinence time), for example, are associated with higher sperm counts, higher semen volumes and a higher percentage of sperm displaying abnormal morphology. Other sources of variability include: scrotal temperature,[3] season of the year,[4] smoking status,[5] marijuana use[6] and geographic region.[7] Although some studies of semen parameter values have attempted to control for some of these variables, many have not, which seriously compromises the conclusions that can be drawn from such studies.

CRITICAL ANALYSIS OF AN INFLUENTIAL PAPER

In 1992, Carlsen *et al.*[8] published a meta-analysis of 61 previous studies of semen parameters and reported a nearly 50% drop in sperm concentrations, from 113×10^6 per ml in 1940 to only 66×10^6 sperm per ml in 1990, and raised the question of whether this 'decline' might be due to exposure to compounds with estrogen-like activity. Although the paper generated a great deal of media attention, it has been repeatedly criticized in the scientific community for its many methodological flaws.[9–13] These flaws include: high cross-study variability in the methods and protocols used for sperm collection and measurement; lack of control for period of abstinence, cigarette smoking or recreational drug use; failure to include some studies reporting no decline in semen parameters; and failure to account for geographic variation between studies.

The pronounced geographic variation in semen quality in particular, is a source of serious error. All of the studies included in the meta-analysis from before 1970 were from the United States, and 80% of these were from New York State, where sperm counts (then and now) are higher than average. After 1970, only three studies were from the United States, and many were from third-world countries where sperm counts were lower than average. If the Carlsen data are reanalyzed to account for this geographic variation, no decline in sperm counts is found (**Figure 1**).[7]

Another potential weakness of the Carlsen study involves the use of an inappropriate linear regression model in the

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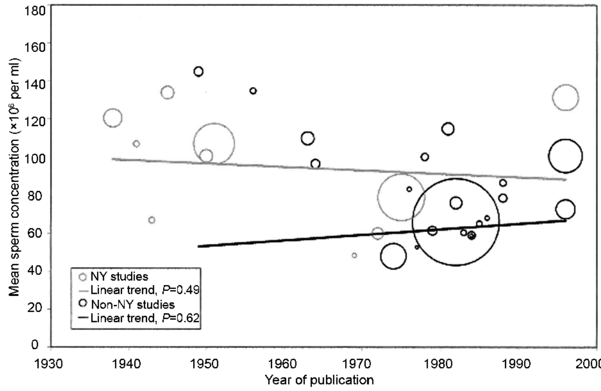

Figure 1 Reanalysis of data from Carlsen *et al.*[8] showing no decline in sperm concentrations (black regression line) when data from New York are excluded. Bubble size corresponds to number of men in study.[9]

statistical analysis.[14] Because the data distribution was highly nonuniform, quadratic or spline regression models are more appropriate analytical tools. When these tools are applied to the Carlsen data, mean sperm concentrations have actually increased since 1940.[12]

In the two decades since publication of Carlsen's paper, at least 35 major studies of time trends in semen parameters have been published. Eight (on a total of 18 109 men) suggest a decline in semen parameter values (**Table 1**); 21 (on a total of 112 386 men) show either no change or an increase in semen quality (**Table 2**); and six (on a total of 26 007 men) show ambiguous or conflicting results (**Table 3**). (Studies that reanalyzed existing data or that were critiques in general ways of some of the methodological issues involved in the debate over alleged changes in semen parameters were not included in this review.) As with previous studies, all of these investigations rely on populations of men who are not necessarily representative of the general male population.

The evidence provided by these studies refutes the simplistic notion of a worldwide decline in semen parameters, though, clearly, they also demonstrate that semen parameter values vary dramatically both geographically and temporally. These variations may arise from numerous causative factors including: differences in lab techniques and analysis between regions; differences in sexual behavior that alter mean abstinence times between regions; genetic variations between populations; variation in lifestyle factors such as obesity or recreational drug use; or variations in *in utero* exposure to mutagenic compounds or environmental pollutants. The wide geographic variations in semen parameter values cannot yet be adequately explained; however, they must be adequately controlled for in any metaanalyses or other attempts to draw broad conclusions about worldwide trends.

To date, however, the data supporting a role for 'endocrine disruptors' in the alleged 'decline' in semen parameters is weak.[15] Some, but not all, studies, for example, have found no association between variations in semen quality and location in rural *vs.* urban areas, or between areas with known high levels of air pollution and those with less pollution.[16] Moreover, a potential causal relationship between semen quality and 'endocrine disruptors' cannot be investigated by studies of semen parameters alone. A recent review of epidemiological studies of

Table 1 Studies showing a decline in semen parameter values (total sample size=18 109)

Year	*First author*	*Sample size*	*Study period*	*Location*	*Major findings*
1995	Auger[19]	1351	1973–1992	France	1. Mean volume: no change. 2. Mean sperm concentration declined 2.1% per year from 89 million per ml to 60 million per ml. 3. Percent motile sperm decreased 0.6% per year. 4. Percent normal sperm decreased by 0.5% per year.
1996	Irvine[20]	577	1984–1995	Scotland	1. Sperm concentration fell from 98 million per ml in older cohort to 78 million per ml among donors born after 1970. 2. Total motile sperm count fell from 169 million to 129 million. 3. Concentration declined 2.1% per year. 4. Motility increased 0.18% per year.
1996	Adamopoulos[21]	2385	1977–1993	Greece	1. Total sperm count declined from 154.3 million to 130.1 million. 2. No significant drop in semen volume.
1998	Bonde[22]	1196	1986–1995	Denmark	1. Median sperm concentration dropped from 63 million per ml in men born 1937–1949 to 52 million per ml in men born 1970 and later. 2. Median total sperm count dropped from 206 million and 117 million respectively.
1999	Bilotta[23]	1068	1981–1995	Italy	1. 31% decline in sperm concentration over the study period. 2. 8% decline in motility. 3. 9% decline in sperm with 'typical morphology'.
2003	Almagor[24]	2638	1990–2000	Israel	1. Sperm count declined by 5.2 million each year. 2. Motility declined by 0.5% per year.
2005	Lackner[25]	7780	1986–2003	Austria	1. Study population was infertile men 2. Decline in sperm concentration from 27.75 million per ml in 1986 to 4.60 million per ml in 2003.
2012	Splingart[26]	1114	1976–2009	France	1. No decline in semen volume. 2. Decrease in total sperm count from 443 million in 1976 to 300 million in 2009. 3. Motility declines from 64% to 49%. 4. Decline in percent of 'normal forms' from 67% to 26%.

Table 2 Studies finding no decline or an increase in sperm count (total sample size=112 386)

Year	*First author*	*Sample size*	*Study period*	*Location*	*Major findings*
1996	Bujan[27]	302	1977–1992	France	1. Sperm counts remained constant after adjustment for age of donors.
1996	Paulsen[28]	510	1972–1993	United States	1. No decreases in sperm count, volume, sperm concentration or normal morphology.
1996	Vierula[29]	5481	1967–1994	Finland	1. Mean sperm concentration unchanged across the study period. 2. Total sperm count and sperm density unchanged. 3. No trends up or down in birth cohort data.
1996	Fisch[7]	1283	1970–1994	United States	1. Sperm concentration increased from mean of 77 million per ml to 89 million per ml. 2. Motility constant, though mean volume decreased slightly.
1997	Berling[30]	718	1985–1995	Sweden	1. Sperm concentration rose from 46 million per ml in 1985 to 64 million per ml in 1995. 2. Sperm with normal morphology rose from 58% to 66.4%.
1997	Benshushan[31]	188	1980–1995	Israel	1. Volume increased 5.1% per year. 2. Total motile sperm count rose 7.7% per year. 3. Motility increased 0.27% per year.
1997	Handelsman[32]	689	1980–1995	Australia	1. Overall mean for period was 69 million per ml. 2. No significant change in semen volume, total sperm count, or sperm concentration over study period.
1997	Rasmussen[33]	1055	1950–1970	Denmark	1. No decline in semen parameters observed over study period. 2. Comparison of four birth cohorts revealed no association with changes in sperm quality.
1998	Emanuel[34]	374	1971–1994	United States	1. No significant differences between mean or median sperm counts between subjects in modern group compared to 1000 subjects in MacLeod and Gold's 1951 study.
1998	Younglai[35]	48 968	1984–1996	Canada	1. Linear regression analysis of the means of each of 11 centers studied over study period showed no significant trend.
1999	Andolz[36]	20 411	1960–1996	Spain	1. 0.04% increase in sperm count per year. 2. 0.4% increase in motility .
1999	Gyllenborg[4]	1927	1977–1995	Denmark	1. Increase in mean sperm concentration from 53 million per ml to 72.7 million per ml. 2. Increase in total sperm count from 166 million to 227 million.
1999	Zorn[37]	2343	1983–1996	Slovenia	1. Volume, concentration and total sperm count did not change in study period. 2. Sperm concentration analyzed by birth cohort showed a decline from 1950 to 1960, then an increase after 1960.
2000	Acacio[38]	1347	1951–1997	United States	1. No decline in sperm concentration found when compared to MacLeod data from 1951 and 1979.
2000	Seo[39]	22 249	1989–1998	Korea	1. Mean sperm concentration was 60.5 million per ml. 2. No change in concentration, volume or motility in study period.
2001	Itoh[40]	711	1975–1998	Japan	1. Volume was unchanged. 2. Sperm concentration was 70.9 million per ml in early study compared to 79.6 million per ml in later.
2002	Costello[41]	448	1983–2001	Australia	1. No significant change in sperm count or ejaculate volume. 2. Increase in sperm motility.
2003	Marimuthu[42]	1176	1990–2000	India	1. No significant decline in sperm counts was observed in any year during the entire study period.
2006	Pal[43]	368	1993–2005	India	1. Mean sperm concentration and semen volume have not decreased in Indian men over the last few decades.
2011	Axelsson[44]	511	2000/2001–2008–2010	Sweden	1. A nonsignificant rise in sperm concentration, from 78 million per ml to 82 million per ml. 2. Nonsignificant increase in total sperm counts from 220 million per ml *vs.* 250 million per ml.
2012	Elia[45]	1327	1992–2012	Italy	1. Sperm concentration, volume and progressive motility significantly higher in 2010 group than 1992 group.

changes in semen parameter values and exposure to endocrine disrupters concluded that convincing human evidence that such exposure has an impact on male fertility is still lacking.[17]

It is worth nothing that, in contrast to the wide variations in results of studies of semen parameter values, studies of temporal trends in testosterone levels have been more uniform. Data from randomized, adequately sized populations of community-dwelling men show a clear and consistent decline in mean testosterone levels in recent decades.[18] Whether such declines are related to the declines in semen quality reported in a minority of studies reviewed here remains to be scientifically explored.

CONCLUSION

The allegations for a worldwide decline in semen parameter values presented by Carlsen *et al.*[8] in 1992 have not withstood scientific scrutiny. This paper, and others,

Table 3 Studies presenting ambiguous results (total sample size=26 007)

Year	First author	Sample size (N)	Study period	Location	Major findings
1995	Comhaire[46]	360	NA	Belgium	1. Motility and morphology exhibited 'highly significant decreases'. 2. Total sperm count did not decrease. 3. 40% of donors after 1990 exhibited 'subnormal' sperm compared with only 5% of group investigated before 1980.
1996	van Waeleghem[47]	416	NA	Belgium	1. Volume increased slightly. 2. Mean concentration declined by 12.4 million per ml in study period. 3. Sperm count was unchanged. 4. Normal morphology decreased from 39.2% in 1977–1980 to 26.6% in 1990–1995.
1996	de Mouzon[48]	7714	1989–1995	France	1. No decline in sperm counts when data were analyzed by year of collection. 2. Sperm counts declined 'regularly' for men born from 1950 to 1975.
1997	Zheng[49]	8608	1968–1992	Denmark	1. Semen quantity and quality did not decline with increasing year of birth during the entire period from 1922 to 1972. 2. From 1950 onward there was a gradual decline in sperm count and normal sperm forms but not in semen volume. 3. Decline in total sperm count was 1.9 million per ml per year of advancing year of birth.
1999	Ulstein[50]	5180	1975–1994	Norway	1. Two subgroups of study subjects showed declines in semen parameters. 2. Subgroup of men with previous children did not show decline in semen parameters.
2010	Mukhopadhyay[51]	3729	1981–1985–2000–2006	India	1. Mean semen concentration rose from 84×10^6 per ml in 1980s to 87×10^6 per ml in 2000s. 2. Volume declined slightly from mean of 2.97 ml to 2.7 ml. 3. Motility declined slightly from 60.6% to 58%.

Abbreviation: NA, not applicable.

have detailed the methodological flaws in the Carlsen paper that warrant its exclusion from future reviews of the data pertaining to variations in semen quality over time. In the two decades since publication of Carlsen's paper, at least 35 major studies of time trends in semen parameters have been published. Eight (on a total of 18 109 men) suggest a decline in semen parameters; 21 (on 112 386 men) show either no change or an increase in semen parameters; and six (on 26 007 men) show ambiguous or conflicting results. The cause (or causes) of the geographical and temporal variations in semen parameters reported by these diverse studies deserve further investigation.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests in relation to this paper.

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