Chapter 40
Are sperm counts declining with time, to what extent and what are the consequences of this decline?

Géraldine Delbès

Since the mid-1970s, there has been continuing global concern regarding the potential for diminishing human reproductive health in industrialized countries. This issue has arisen in part in the context of the revision of minimum semen quality standards and some observations of declining sperm concentration over time in men. These reports have led to the worry that “something has altered the fertile male population to depress the semen quality remarkably"(Nelson & Bunge, 1974, p. 507). The hypothesis of sperm decline was further supported by a 1992 meta-analysis of 61 studies of human semen quality published during a 50-year period (1938-1991), representing almost 15,000 men from among 20 different countries; an approximately 50% decline in sperm counts (113 to 66 million/ml) was found over that time frame. Additional concern about a temporal (secular) decline in semen quality was heightened by a 1995 French publication that reported a 30% decrease in sperm concentration (89 to 60 million/ml) from among Parisian sperm donors during a 20-year period (1970- 1992).

Thereafter, a large number of additional studies, reviews and editorials ensued to support or reject the concept that “male fertility”, as measured by sperm concentration, was in fact changing. the scientific community raised substantive questions about the validity of the data. Criticisms regarding the conclusions in some papers that there are global secular changes in semen quality are based on numerous issues known to profoundly affect semen quality. These include: 1) lack of standardized criteria for semen sample collection, 2) bias introduced by using different counting methodologies, 3) inadequate within- individual semen sampling in the analysis, 4) failure to account for variable abstinence intervals and ejaculatory frequency, 5) failure to assess total sperm output rather than concentration, 6) failure to assess semen parameters other than the number of sperm, 7) failure to account for age of

subject, 8) subject selection bias among comparative studies, 9) inappropriate statistical analysis, 10) ignoring of major geographic differences in sperm counts, and 11) the casual equating of male fertility with sperm count per se.

In 2017, Levine et al. re-evaluated the question, addressing many of the above-mentioned methodological criticisms in a meta-analysis of 185 studies of human semen quality published between 1981 and 2013, representing 42,935 men from 50 different countries, who provided semen samples between 1973 and 2011. Using a meta-regression model, they reported a decline of 0.75% per year in sperm concentration and total sperm count for all men. This decline was the most pronounced in unselected men from Western countries (North America, Europe, Australia, and New Zealand) with 1.4% per year in sperm concentration and 1.6% per year in total sperm count. A similar but less steep negative slope was observed for selected fertile Western men. Overall, 59.3% decline in total sperm count (337.5 to 137.5 million) was found between 1973 and 2011 in the unselected western population. Interestingly, when separating data for other countries (South America, Asia and Africa) no significant trend were seen either in the unselected population or fertile men. Yet, since this meta-analysis, systematic reviews of Chinese, African or Indian populations, among many others, have also reported a decline in sperm concentration over time, with an approximately similar trend of ~1% decline per year. In 2022, a worldwide meta-analysis has validated these findings

The concordance of several strong meta-analyses reinforces and rally the scientific community on the fact that the sperm count is decreasing. Interpretation of the consequences yet remains. The media has seized on these data to conclude that there is a decrease in male fertility, and to question the causes. Indeed, sperm concentration is one of the determinants of fertility of an individual. According to the reference criteria established in 2021 by the WHO, the threshold of 10 million spermatozoa per ml can define infertility (Chapters 22, 32). The significance of the conclusion of a decline in sperm count worldwide therefore appears to be an alarm signal for the reproduction and survival of the human species. Concerns that environmental toxicants such as endocrine disrupting chemicals, as well as obesity, diet and lifestyle changes, may be impacting human reproductive health are likely to be important considerations. Support for such concerns comes from parts of Europe where there is now evidence for increasing incidence of testicular cancer, and

congenital genito-urinary abnormalities (hypospadias, cryptorchidism) as well as secular, age-independent decline in serum total testosterone and sex hormone binding globulin in both age-matched Danish and American men. The shared risks for these testicular disorders have led to the concept of a "Testicular Dysgenesis Syndrome" that might include downstream changes in semen parameters (Chapter 44). In short, this hypothesis suggests that alteration of the *in-utero* environment may be the common cause of these male reproductive abnormalities, leading to an overall decrease in human fertility.

Recently, Boulicault *et al.* presented the "sperm count bioavailability" hypothesis providing an alternative, more inclusive, framework for interpreting the global sperm count decline as described by the Levine report from 2017. This framework is based on the following principles: 1) above the WHO threshold, a high average sperm count is not necessarily optimal; 2) there is no species-typical reference in the 1970s; 3) semen parameters vary considerably within an individual or a population because ejaculate is an excretory product that is influenced by many external conditions without necessarily being associated with fertility or health hazard. While it does not rule out the possibility that the decline may have implications for population fertility, this analysis puts into perspective the significance of the overall decline from "normal" to "normal" sperm concentration by WHO criteria, suggesting that these trends may be due to benign or adaptive variation depending on a variety of individual and most of all geographic factors.

Based on the above discussion, it can be concluded at this time that there is a global temporal downward variation in human sperm count. However, the causes of this variation and its significance in terms of male fertility and men's health remain debatable. Indeed, regional differences in sperm count have not yet been explained and deserve further study. Moreover, the assumption that this decline will continue linearly over time remains hypothetical. The recent analysis of more contemporary data from 2000 onward suggests that the downward slope is getting steeper. In addition, the contribution of environmental causes including lifestyle changes and xenobiotics is suspected and strongly supported by experimental studies, yet, it still requires precise longitudinal prospective epidemiological studies. Because of the variability of semen analysis parameters, the statistical power of these studies requires large cohorts controlling for multiple confounding factors

making them difficult to do. Yet, these studies are heavilly needed to better understand the causes of sperm count decrease in Human and to determine the actual consequences on male fertility.

Suggested reading

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