

## Is there a decline in sperm counts in men?

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Over a number of decades now, there has been continuing global concern regarding the potential for diminishing human reproductive health in industrialized countries. This has been supported by the discovery of congenital genito-urinary defects among some lower species exposed to industrial toxicants in the environment. Of particular concern were the “estrogen-mimics” (xeno-estrogens) because of their potential to disrupt cellular and physiological functions, even in minute doses. This gave birth to the concept that exposure to such “endocrine disruptors” could produce clinically detectable changes in human reproductive functions; in-utero and early exposures being the potential cause of long term male reproductive disorders.

The credibility of this hypothesis was 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 23 different countries; an approximately 50% decline in sperm counts (113 to 66 million/ml) was found over that time frame. Further concern about a temporal (secular) decline in semen quality was heightened by a 1995 French publication that reported a 30% decrease in sperm counts (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 count, was in fact changing. However, among the aggregate research reports, only a few showed unambiguous declines in semen quality; most studies found no decline, an increase or mixed changes in semen parameters (Chapter 12). Nevertheless, the worrisome concern that human “male fertility” was diminishing was kept in the headlines primarily by the media that focused on only a portion of the data (declining sperm counts); while the scientific community raised substantive questions about the validity of the data as detailed below.

Among the many reported studies, 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.

Unlike the tight homeostatic regulation of blood component levels in the internal milieu, semen parameters vary considerably because the ejaculate is an excretory product that is influenced by many external conditions. Ejaculatory frequency and abstinence interval are major determinants of sperm output and semen quality. With prolonged intervals between ejaculations (days), sperm output increases due to higher caudal epididymal reserves, but motility and normal morphology values decrease. Seminal fluid volume is also highly variable between and within individuals; thus, only total sperm output adequately quantifies sperm number in the ejaculate. In addition, it is well known that even under standardized conditions of semen collection there is marked variability of within-individual sperm counts (75% coefficient of variation), such that at least three semen samples are generally required to obtain a stable estimate of semen parameters. Thus, retrospective studies that assess only one semen sample collected under non-standardized conditions are seriously flawed. In addition, semen quality diminishes considerably with advancing paternal age. Since the age of subjects reported in the various studies extends over many decades, comparisons of such data between groups must be done with great caution.

Over and above the technical concerns regarding interpretation of the reported semen analyses, subject selection bias among the studies appears to be an even more critical issue. Within some publications, study subjects included younger sperm donors, older pre-vasectomy patients or patients attending infertility clinics. None of these groups are representative of the general population, and within each subject group, selection criteria are not defined and may have varied significantly over the time frame of the study.

An additional factor that has yet to be adequately explained is the marked difference in sperm counts reported from differing geographic regions even within the same country. An inclusive analysis of all 29 available reports of sperm counts from only the United States during almost 60 years (1938-1996) revealed a statistically significant secular decline. However, sperm concentrations from the four publications involving subjects living only within New York cities were significantly higher (30%) compared to all other U.S. cities and there was no statistical difference in values reported from among the four New York cities. When the New York data were eliminated from analysis of the remaining 25 studies, no temporal decline in sperm counts was evident. Most critically, re-analysis of the 1992 meta-analysis of 61 studies of sperm counts revealed that no secular decline was

evident when the four earlier New York data sets were eliminated.

Given the above discussion, it seems impossible at present to scientifically conclude that there is or is not a worldwide secular decline in human sperm counts or male fertility. However, the regional differences in sperm counts have yet to be explained and deserve further investigation. In addition, assessments of sperm quality other than count, motility and morphology need consideration as a measure of male fertility potential. Recent studies of sperm chromatin structure may be relevant. Concerns that environmental toxicants, as well as obesity 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 an increasing incidence of testicular cancer, and preliminary evidence for congenital genito-urinary abnormalities (hypospadias, possibly 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 33).

### **Suggested reading**

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