VIEWPOINT
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Environmental interference and declining male fertility

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ABSTRACT

Declining human male 'fertility' has been equated with a temporal decline in sperm counts, with reports collectively spanning the period between 1934 and 2018. Although sperm quality is impacted by adult male lifestyle choices, e.g. diet, stress and exposure to heat, environmental factors are thought to be central to this alarming observation. Since the decline in sperm counts reflects the outputs of meta-analytical studies, and thus the combination of data from different laboratories, statistical models have had to control for potential confounders, including differences in laboratory methodologies, changes in quality assurance standards, age, fertility group and exclusion criteria indicators. Sperm analyses arising from a population of stud dogs, where all analyses were carried out in a single laboratory, demonstrated a 30% decline in sperm motility over 26 years. Since these dogs resided in normal homes and were therefore exposed to the same household environment as human cohabitees, it has been postulated that the temporal decline in both dog and human sperm quality reflects environmental interference. This viewpoint article explores this contention and its implications for male 'fertility'.

Keywords: dog, environmental, environmental chemicals, fertility, male, sentinel, sperm count, sperm motility.

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Despite considerable progress in our understanding of the biology of gonadal development and function, a new layer of complexity has emerged in the alarming form of environmental interference, mediated by anthropogenic pollutants and pharmaceuticals. Over the last 4–5 decades, the numbers of publications providing evidence of pollutant effects on male and female reproductive development, function and fertility has increased exponentially and, in parallel, public awareness and concern around declining reproductive health has similarly increased. An alarming contention central to this area is the longer-term implications of an ongoing decline in 'fertility'. Inevitably, this is widely debated in scientific, medical and more populist circles, with diverging opinions on the seriousness of such a contention. In order to explore this further, one must first define the term 'fertility' and how this differs from frequently cited indices of fertility in the literature.

The consensus definition of fertility is 'the capacity to establish a clinical pregnancy' (Bhattacharjee *et al.* 2024). Since a decline in sperm quality (count, motility) may theoretically reduce this capacity, association studies generally rely on this inference. A commonly cited index of fertility in humans is the Total Fertility Rate (TFR), for which data is easily available from the World Bank. TFR is defined as 'the number of children that would be born to a woman if she were to live to the end of her childbearing years and bear children in accordance with age-specific fertility rates of the specified year' (Vander Borght and Wyns 2018; Bhattacharjee *et al.* 2024). Although a practical and useful metric, the numbers quoted are influenced by a multitude of factors, including social, economic, educational and lifestyle influences (De Jonge *et al.* 2024). For example, in the Western World, many couples make the choice to start families later in life, when the risk of compromised fertility is elevated. Other lifestyle choices will also have negative effects, such as poor diet, stress, urbanisation and exposure to heat (De Jonge *et al.* 2024). It follows, therefore, that altering these elements of lifestyle may improve fertility prospects. However, once these choice elements are removed, we begin to approach the true problem of infertility.

Defined in humans as the inability to establish a clinical pregnancy after 12 months of regular and unprotected intercourse, infertility affects approximately one in six people globally (WHO 2023). Males and females are reported to be solely responsible for 30% of cases each and, in a further 30% of cases, both partners are responsible, leaving 10% of cases unexplained. Reproductive disease affecting both or individual genders has been extensively reviewed elsewhere (Vander Borght and Wyns 2018; Carson and Kallen 2021). The following is a personal perspective around temporal trends in male fertility and its potential linkage with environmental interference.

For more than 50 years, there have been numerous reports on human semen quality, and these have been subject to meta-analytical studies. Those outlined in Table 1 illustrate the chronology of those studies most widely cited. Five of these studies collectively conclude that human semen quality, primarily sperm counts, have declined between the years of 1934 and 2018 (Carlsen *et al*. 1992; Swan *et al*. 2000; Rolland *et al*. 2013; Levine *et al*. 2017, 2023). In one additional study, Tiegs and colleagues report a decline in total motile sperm count based on just under 120,000 men presenting at two infertility clinics (Tiegs *et al*. 2019).

Despite the publication of these meta-analytical studies over 30 years, concerns continue to be raised around the validity of comparing data from different laboratories across decades, with differing degrees of quality assurance (Pacey 2013; Bjorndahl *et al*. 2022). The picture is further complicated by changes in WHO reference ranges by which a diagnosis of sub-fertility is made, by a generalised bias in the pre-2023 studies to data primarily collected from Western society countries and in studies showing no temporal decline in sperm quality (Cipriani *et al*. 2023; Kimmins *et al*. 2024). To overcome these confounders and conflicting reports, the most extensive meta-analysis to date included data from South and Central America, Asia and Africa and alarmingly, reported that the rate of decline of human sperm counts doubled after the year 2000 from 1.16% to 2.64% per year (Levine *et al*. 2023).

Despite the most advanced statistical modelling being used to control for the many possible confounders inherent in a meta-analytical study, that there is any doubt at all dictates the need for a different and complimentary strategy. Such an approach comes from studies of household dogs that are exposed to the same environmental factors as human cohabitees. Specifically, access to a population of stud dogs used as part of a breeding programme to generate support dogs for blind and partially sighted people, provided an ideal cohort free of the many challenges of human studies. The dogs enrolled in the programme live in the homes of the people they support, they are fed controlled diets, and they are routinely monitored for sperm quality and reproductive health. Analyses of historical sperm data has demonstrated a 26-year decline in sperm motility between the years of 1988 and 2014 (Lea *et al*. 2016). Notably, data used in this 'non-meta-analytical' study was generated from a single laboratory, using consistent techniques employed by three

Table 1. Large scale analyses investigating temporal trends in human semen quality.

Publication	Parameter	Type of study	Population	Conclusion
Carlsen *et al*. (1992)	Sperm count	Meta-analysis	14,947 men, 61 papers (no history of infertility)[A]	Decline: 1940–1990 113×10^6–66×10^6/mL
Rolland *et al*. (2013)	Sperm count	Fivnat database (France)	154,712 men, partners of couples undergoing assisted reproductive technology treatment across France	Decline: 1989–2005 73.6×10^6–49.9×10^6/mL
Levine *et al*. (2017)	Sperm count	Meta-analysis	42,935 men, 185 papers (unselected by fertility status and proven fertility)[B]	Decline: 1973–2011 99×10^6–47.1×10^6/mL (unselected)
Tiegs *et al*. (2019)	Total motile sperm count	Two centres	119,972 men presenting at infertility centres	Decline: 2002–2017 10% decline
Swan *et al*. (2000)	Sperm count	Meta-analysis	Carlsen 1992 data expanded. 101 papers	Decline: 1934–1996: decline similar to Carlsen study
Levine *et al*. (2023)	Sperm count	Meta-analysis	57,168 men, 223 papers (unselected by fertility status and proven fertility)[C]	Decline: 1973–2018 103.7×10^6–49.1×10^6/mL (unselected)
Cipriani *et al*. (2023)	Sperm count	Meta-analysis	24,196 men, 62 articles (fertile, young and old unselected by fertility status)	No decline in USA and selected western countries.

[A]North America mostly + Europe.
[B]Western + South America, Asia, Africa.
[C]North America–Europe–Australia, South/Central America–Asia–Africa.

technical staff. More recently, a preliminary extended data analysis indicates that after controlling for hereditary effects, the decline has continued to the present day: a period of 35 years (McCrum *et al.* 2025).

In broad terms, environmental interference is indicated by (1) the rapid temporal decline in sperm quality (human and dog), (2) a co-incident increase in the occurrence of testicular germ cell cancer in younger men (human), (3) rising incidences of cryptorchidism in newborns (human, dog) and (4) a higher incidence of these parameters in industrialised areas (Lea *et al.* 2016; Skakkebaek *et al.* 2016; Le Moal *et al.* 2021). Consequently, it was proposed that these observations had a common aetiology and were linked as testicular dysgenesis syndrome (TDS). That is, TDS is programmed by environmental interference that occurs *in utero* as a form of programming (Skakkebaek *et al.* 2001). In support of this, earlier comparative human studies described an elevated incidence of TDS in men from urban Denmark versus those in rural Finland (Jørgensen *et al.* 2002, 2006). More recent human reports, however, indicate that semen quality and the incidence of testicular cancer in men from Finland has now converged with those in Denmark, indicative of elevated environmental interference in Finland (Rodprasert *et al.* 2019).

Given the routine practice of removing testes from pet dogs for the purpose of surgical contraception, the consented use of residual testicular tissue provides an unlimited source of tissue for exploring testicular pathologies and for determining whether environmental chemicals are detectable in the gonad itself. Consequently, the examination of pet dog testes from the UK, Denmark and Finland has shown international differences in the degrees of testicular pathology and in the profile of contaminants detected (Sumner *et al.* 2021). Although, these studies do not demonstrate causality, they do support the concept of the household dog as a sentinel species for the examination of environmental interference on human male reproductive function.

Collectively, although the evidence of a temporal decrease in male fertility is compelling, the demonstration of causality remains elusive. A series of elegant experiments carried out in pregnant rats, has however shown that exposure to an anti-androgenic chemical (flutamide) during a highly sensitive pre-natal male programming window, induces a TDS phenotype that closely approximates that reported in the human (Welsh *et al.* 2008). This was also shown using the anti-androgenic chemical dibutyl phthalate (DBP) (Van den Driesche *et al.* 2017). Furthermore, dog and human sperm exposed *in vitro* to individual environmental contaminants at concentrations known to be present in the dog testis, exhibit reduced motility and increased DNA fragmentation (Sumner *et al.* 2019). Consequently, both the developing fetus and adult are sensitive to environmental interference.

Although anthropogenic pollutants (e.g. phthalates, pesticides, flame retardants, polychlorinated biphenyls, per- and polyfluoroalkyl substances) and analgesics (e.g. paracetamol, ibuprofen) capable of environmental interference have been identified, the reality is that; (1) real-life exposure is to mixtures of chemicals and drugs, (2) within a mixture, chemicals and drugs may interact (additive, synergistic, antagonistic), (3) metabolic break-down products produced *in vivo* (and *in vitro*) may also be implicated in a biological effect. Furthermore, the linkage of poor sperm quality to overall adult health has implications beyond fertility (Capelo *et al.* 2024; De Jonge *et al.* 2024).

In conclusion, it is now generally accepted that (1) male sperm quality, reflective of fertility, is declining globally and (2) Western lifestyle choices account for a proportion of these cases. Once the element of choice is removed, the weight of evidence points to inadvertent and deliberate exposure to anthropogenic pollutants and analgesics as a broad mechanism underlying the decline. It is therefore imperative that further funds are channelled to establish causality, mechanism and to mitigate environmental effects on fertility and long-term health.

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