Male fecundity and its implications for health and disease across the lifespan

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In this issue of Human Reproduction, Eisenberg et al. (2014) provide empirical evidence in support of the evolving literature suggesting that human fecundity influences health and disease across the lifespan. Human fecundity is defined as the biologic capacity of men and women for reproduction irrespective of pregnancy intentions (Buck Louis, 2011), and is typically measured by end-points such as hormonal profiles and semen quality in men or pregnancy in couples. Increasingly, however, investigators recognize fecundity’s possible implications beyond the narrowly defined sensitive window of human reproduction to include health and disease across the lifespan. Included in this conceptual paradigm is the assumption that fecundity impairments may be in the pathway to later onset disease, possibly having a shared etiology. To this end, human fecundity may be both informative and predictive about continual health status and later onset disease, as postulated in the testicular dysgenesis syndrome paradigm (Skakkebaek et al., 2001). This paradigm considers the interrelatedness of a spectrum of male fecundity endpoints in relation to purported etiologies. Of further note is the possibility of trans-generational effects associated with impaired male fecundity, as suggested by cryptorchid boys being more likely to have fathers with lower median sperm counts and concentrations than unaffected boys (Asklund et al., 2007).

Eisenberg et al. (2014) provide evidence in support of a relation between semen quality and mortality among US men who sought infertility evaluation at two geographic sites in the USA. Despite the relatively young ages of men, mortality was higher for men with severely impaired semen quality or male factor infertility in relation to men with normal semen quality. In particular, men with low seminal volume, sperm concentration, motility and count, as defined by the World Health Organization 5th edition (Cooper et al., 2010), were at higher risk of mortality than unaffected men. The overall conclusions of an adverse relation between semen quality and male mortality remained even when considering current health status and a combination of two or more parameters indicative of poor semen quality.

What is particularly concerning about the findings is the observation of greater mortality for affected compared with unaffected men in a short period of time following the infertility evaluation. This finding begs the question as to whether or not a higher likelihood of mortality remains across the lifespan for men with suboptimal semen quality. If such a relation exists, what is the cause(s)? Immediate suspects include environmental factors such as obesity and physical inactivity or chemicals, all of which have been associated with semen quality and health status. Critics of these recent findings will be quick to point out the important limitations underlying this work, including its ecologic study design that relies upon linkages between infertility clinics and the U.S. Social and Security Death Index, the absence of information on behaviors that may be associated with premature mortality or cause specific mortality, a relatively short follow-up period (7.7 years) in the context of a small absolute number of deaths (<1%), and other limitations that typically accompany observational research.

Despite such limitations, Eisenberg and colleagues’ (2014) findings are consistent with those reported by previous authors who assessed men seeking clinical services (Groos et al., 2006; Jensen et al., 2009). The former study assessed sperm concentration and mortality, which was ascertained through vital registration data. Mortality was reportedly 2-fold higher for oligozoospermic men in comparison to normozoospermic men, prompting the authors to conclude a relation between diminished fertility status and life expectancy. Jensen et al. (2009) noted an inverse relation between sperm concentration (up to 40 million/ml), motility and morphology in 43,277 men undergoing semen analysis and mortality as identified through population-based record linkages. While not directly comparable, the findings for diminished semen quality and mortality are consistent with those reported for childless men and cardiovascular mortality in a large sample of US men (Eisenberg et al., 2011).

In moving forward, two unresolved questions emerge. Firstly, how robust will the findings be in a general population of men not seeking infertility services? And secondly, how should semen quality and health and disease across the life course be modeled if indeed a shared etiology is suspected? Moreover if semen analysis is non-informative for predicting couple fecundity or fertility as suggested by some authors (Lefèvre et al., 2007; Niederberger, 2011), might it have relevancy for male health across the life course? If so, should all men be ‘screened’ and encouraged to adopt or maintain lifestyle conducive to both good semen quality and health? At present the answer to this question is unknown, but the...
findings reported in this exciting paper coupled with the existing, albeit limited, literature support concerted efforts to better understand the interrelated and perhaps conditional nature of male fecundity and health across the lifespan. If the temporal pattern for declining semen quality is true as reported by some but not all authors (Jørgensen et al., 2012; Le Moal et al., 2014), what are the implications for men’s health, globally? There is no better time than the present to open our thinking to such investigation!

References


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