

Paternal age over 51 years reduces success rate in IVF and ICSI

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While female fertility comes to an irrevocable end with the menopause (at a consistently average age of 51 years), men are not constrained by similar biological senescence. Studies have shown that sperm counts may decline and DNA damage in sperm cells may increase over time, but the celebrity fatherhood of ageing actors and rock stars perpetuates the myth that male fertility might last forever.

However, the published evidence does show that men are indeed regulated by a biological clock. Studies have demonstrated a decline in natural male fertility and an increase in miscarriage rate as men get older. So far it is not yet known whether [paternal age](#) affects outcomes in IVF and ICSI—or if there is (or should be) any age limit to treatment.

Now, an analysis of almost 5000 IVF/ICSI cycles performed at a single centre in London indicates that success rates do decline significantly after a paternal age of 51 years. Miscarriage rate in this study was not affected by the age of the male partner. Nevertheless, the investigators confirm that paternal age over 51 does significantly affect the chance of success in assisted reproduction, adding that this warrants a call for 'a public health message for men to not delay fatherhood.'

The results of the study are presented today by Dr. Guy Morris from the Centre for Reproductive and Genetic Health (CRGH) in London, where this observational retrospective study was performed. The research team from CRGH and the Institute for Women's Health at University College London analysed the records of 4271 men involved in 4833 cycles of IVF and ICSI treatment for all causes of sub-fertility between 2009 and 2018. The male partners were grouped into age ranges of 35 and under, 36-40, 41-44, 45-50, and over 51 years for analysis. A male age and female age under 35 years were used as reference control groups for comparison.

The analysis first showed that fewer men over 51 met the standard WHO semen reference values than did men under 51 (42.1% vs 61.1%). It was similarly found—as expected—that clinical pregnancy rate declined with increasing maternal age over 35 years—from 51.1% for under-35s to 21.7% for over-40s. Both these trends were statistically significant.

The study also showed that clinical pregnancy rates declined with increasing paternal age—from 49.9% in the under 35 group, to 42.5% in the 36-40s, to 35.2% in the 41-45s, to 32.8% in the 46-50s, and to 30.5% in the over 51s. These results were re-analysed in a statistical model which included maternal age and it was found that, for all maternal age subgroups, the probability of pregnancy still decreased significantly with paternal age over 51 years.

Dr. Morris and his colleagues noted that 80% of the cohort's couples with male partners over 51 were treated with ICSI, a treatment developed for male infertility and requiring just one viable sperm cell for fertilisation. However, although 42% of these older male partners did have normal semen parameters (sperm count, sperm motility), he points out that 'this may have confounded the results and reduced the perceived effect of increased paternal age.'

Commenting on these results, Dr. Morris said: "There may well be a public perception that [male fertility](#) is independent of age. Stories of celebrity men fathering children into their 60s may give a skewed perspective on the potential risks of delaying fatherhood. Indeed, in natural conception and pregnancy it is only recently that evidence of risks associated with later fatherhood has become available. These more recent studies contrast with decades of evidence of the impact that maternal age has on fertility outcomes.

"In the context of this emerging evidence for the deleterious effect of increasing paternal age, our

data certainly support the importance of educating men about their fertility and the risks of delaying fatherhood."

This study was observational and not designed to investigate any biological explanation for its findings. However, Dr. Morris said that the data 'suggest that semen quality decreases with increasing age and that this decline mirrors the decline in IVF outcome which we found.' It's for this reason, he explained, that some centres limit the age of their sperm donors (usually up to the age of around 40). While some clinics and health authorities set an upper age limit on female IVF patients, no such limits are known to exist for males.

More information: Abstract O-304, Wednesday 26 June 2019: Paternal age over 50 years reduces the success of IVF/ICSI - ET

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