



The
Fertility Society
of Australia

Pre-conception Health Special Interest Group



Age, fertility and assisted reproductive technology

In most high-income countries the age of childbearing is increasing. In Australia the average age of all women who gave birth was 30.1 years in 2013, compared with 29.5 in 2003. The average age of first time mothers also increased, from 27.8 years in 2003 to 28.6 in 2013 [1]. Over the last decade, peak fertility rates have shifted from women in the 25-29 year age group to the 30-34 year age group [2]. Between 1990 and 2010, the median age of fathers of nuptial births increased by almost three years, from 31.4 to 34.0 years [3]. The evidence about the impact of parental age on fertility and ART outcomes is discussed here.



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A systematic review of 297 articles reports the following as underlying reasons for women postponing childbearing:

- effective contraception and control of reproduction
- education and career pursuit
- women's labour force participation and incompatibility of childcare and participation
- ideational shifts in values concerning reproduction
- issues of gender equity such as the greater restrictions to women's career opportunities imposed by reproduction compared to men
- the stability of partnerships and ability to find a partner who will participate in reproduction and parenting
- ability to establish oneself in relation to employment, housing
- general economic uncertainty [4].

Globally there is an increasing population of women of advanced reproductive age seeking assisted reproductive technology (ART) treatment due to age-related infertility. However it is widely accepted that ART cannot compensate for the natural age-related decline of fertility [5].

Several studies show that women and men underestimate the impact of age on fertility and the ability to conceive [6-8]. Other studies have found that women overestimate the capacity of ART to overcome age-related infertility [9-10].

Evidence review

Female age and fertility

Studies of populations where virtually no birth control is practised demonstrate that fertility begins to decline from age 25 [11-12]. This is due to a decline in oocyte quality such as aneuploidy rather than merely decreasing oocyte numbers [12]. The decline in oocyte quality becomes clinically relevant for women from their mid-30s [11-12]. The prevalence of infertility increases from 1% at age 25 to 55% at age 45 [12]. While 75% of women attempting conception at age 30 conceive within 12 months, by age 40 this has declined to 44%. Further, 20% of women who conceive at age 35 will have a spontaneous abortion. The monthly fecundity resulting in live-birth rate among women aged 30, 35 and 40 year is 17%, 12%, and 5% respectively [12].

Male age and fertility

Recent reviews have concluded that increased male age is a risk factor for infertility [14-17]. The aetiology of declining male fertility is related to falling androgen levels, decreased sexual activity, alterations in sperm motility and morphology, and deterioration in sperm quality and DNA integrity [14-15, 17]. Time to pregnancy (TTP) increases with increasing male age [13-17]. When controlling for other factors that may influence TTP, it has been shown that TTP increases when the male partner is 45 or older [13-14]. Increased male age is also associated with increased risk of spontaneous abortion and diseases of complex aetiology in the offspring such as schizophrenia, autism spectrum disorders, autosomal dominant inherited diseases and Trisomy 21 [16-17].

Age and assisted reproductive technology (ART) outcomes

Maternal age is the single most important prognostic factor for ART success [4, 19-21]. Studies that have investigated retrospective data concerning female age and the outcome of ART show that the chance of pregnancy declines with age and the incidence of pregnancy loss increases [4, 19-20].

In 2012 the average age of women in Australia and New Zealand who underwent ART treatment using their own oocytes was 35.8 years [21]. The live delivery rate per fresh cycle was 26% among women aged under 30 and less than 1% in women aged 44 or older [21].

Some studies report that women over the age of 40 can have a greater than 5% chance for success in ART but no pregnancies are reported for women aged 46 or more who are using their own oocytes [18-20]. In a study conducted by Klipstein et al [18] the outcome of the first IVF cycle in older women did not predict the outcome of subsequent cycles.

Although some studies have found a negative relationship between paternal age and ART success [13-15] a 2011 review concluded that there is currently insufficient evidence to demonstrate a negative effect of paternal age on ART outcomes [22].

Women who conceive with ART after the age of 40 have a greater risk of miscarriage, gestational diabetes, pregnancy-induced hypertensive disorders, instrumental deliveries and caesarean sections than younger women [11].

Summary

Maternal and paternal ages both influence fertility and the chance of having a live birth. Time to pregnancy (TTP), and the risk of infertility, spontaneous abortion, ectopic pregnancy and chromosomal abnormalities increase in women from about age 30 with more pronounced effects in women aged over 35. The effects of a woman's age are compounded by the effects of age in their male partner. The risk of preterm births and stillbirth increases from paternal age 35 with more pronounced effects from age 40. Male fertility starts to decline at about age 45 and the risk of fathering a child with developmental problems including autism spectrum disorders increases after age 40.

Recommendations

- Physicians need to consider both the age of the woman and her male partner (if applicable) when discussing ART treatment and possible outcomes.
- The chance of ART success in women aged over 44 using their own eggs is negligible.
- Public education about the relationship between age and fertility in both women and men is needed.
- In public information there needs to be greater emphasis on the failure of ART to treat age-related infertility.

For more information about pre-conception health visit


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References

1. Australian Institute of Health and Welfare 2015. "Australia's mothers and babies 2013—in brief." Perinatal statistics series no. 31. Cat no. PER 72. Canberra: AIHW.
2. Australian Bureau of Statistics 2015. "3301.0 - Births, Australia, 2014." Canberra, Australian Bureau of Statistics.
3. Australian Bureau of Statistics 2011. "3301.0 - Births, Australia, 2010." Canberra, Australian Bureau of Statistics.
4. Mills, M., Rindfuss, R., McDonald, P. and te Velde, E. 2011. "Why do people postpone parenthood? Reasons and social policy incentives." *Human Reproduction Update* 17, 848-860.
5. de Graaff, A.A., Land, J.A., Kessels, A.G.H., Evers, J. 2011. "Demographic age shift toward later conception results in an increased age in the subfertile population and an increased demand for medical care." *Fertility and Sterility*, 95(1): p. 61-67.
6. Brethrick, K., Fairbrother, N., Avila, L., Harbord, S. and Robinson, W. 2012. "Fertility and aging: do reproductive-aged Canadian women know what they need to know?" *Fertility and Sterility* 93, 2162-2168.
7. Peterson BD, Pirritano M, Tucker L, Lampic C. 2012. "Fertility awareness and parenting attitudes among American male and female undergraduate university students." *Human Reproduction*, 27:1375-08.
8. Hammarberg, K., Setter, T., Norman, R., Holden, C., Michelmores, J. and Johnson, L., 2013. "Knowledge about factors that influence fertility among Australians of reproductive age: a population-based survey." *Fertility and Sterility*, 99:2, 502-507.
9. Maheshwari, A., Porter, M., Shetty, A. and Bhattacharya, S. 2008. "Women's awareness and perceptions of delay in childbearing." *Fertility and Sterility* 90, 1036-1042.
10. Hashiloni-Dolev, Y., Kaplan, A. and Shkedi-Rafid, S. 2011. "The fertility myth: Israeli students' knowledge regarding age-related fertility decline and late pregnancies in an era of assisted reproduction technology." 26:11, 3045-53.
11. Homan, G., Davies, M. and Norman, R. 2007. "The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment: a review." *Human Reproduction Update* 13, 209-223.
12. Schmidt, L., Sobotka, T., Bentzen, J. and Andersen, N. 2011. "Demographic and medical consequences of the postponement of parenthood." *Human Reproduction Update* 18, 29-43.
13. Kidd, S.,Eskanazi, B. and Wyrobek, A. 2001. "Effects of male age on semen quality and fertility: a review of the literature." *Fertility and Sterility* 75, 237-248.
14. de La Rochebrochard, E.,Mouzon, J.,Thepot, F,Thonneau, P. and French National IVF Registry Association 2006. "Fathers over 40 and increased failure to conceive: the lessons of in vitro fertilization in France." *Fertility and Sterility* 85, 1420-1424.
15. Sartorius, G. and Nieschlag, E. 2010. "Paternal age and reproduction." *Human Reproduction Update* 16, 65-79.
16. Kuhnert, B. and Nieschlag, E. 2004. "Reproductive functions of the ageing male." *Human Reproduction Update* 10, 327-339.
17. Wiener-Megnazi Z, Auslender R, Dirnfeld M. 2012. "Advanced paternal age and reproductive outcome." *Asian Journal of Andrology* 14: 69-76.
18. Klipstein, S., Regan, M., Machtinger, R., Ryley, D., Goldman, M., Alper, M. and Reindollar, M. 2005. "One last chance for pregnancy: a review of 2,705 in vitro fertilization cycles initiated in women age 40 years and above." *Fertility and Sterility* 84, 435-445.
19. Hourvitz, A., Machtinger, R., Maman, E., Baum, M., Dor, J. and Levron, J. 2009. "Assisted Reproduction in women over 40 years of age: How old is too old?" *RBM Online* 19, 599-603.
20. van Loendersloot, L., van Wely, M.,Bossuyt, P., Repping, S. and van der Veen, F. 2010. "Predictive factors in in vitro fertilization (IVF): a systematic review and meta-analysis." *Human Reproduction Update* 16, 577-589.
21. Macaldowie, A., Y. A. Wang, et al. 2014 . "Assisted reproductive technology in Australia and New Zealand 2012." Assisted reproduction technology series no.16 National Perinatal Epidemiology and Statistics Unit, the University of New South Wales: Sydney.
22. Dain, L., Auslander, M. and Dirnfeld, M. 2011. "The effect of paternal age on assisted reproduction outcome." *Fertility and Sterility* 95, 1-8.