Asian Journal of Andrology (2016) 18, 425

www.asiaandro.com; www.ajandrology.com

Open Access

INVITED COMMENTARY

Male Aging

The role of advanced paternal age in modern reproductive medicine

Christopher Wu[1], Larry I Lipshultz[2], Jason R Kovac[3]
Asian Journal of Andrology (2016) **18**, 425; doi: 10.4103/1008-682X.179251; published online: 8 April 2016

In recent years, there has been a significant trend toward postponing childbearing, especially in developed countries. There are multiple factors influencing this change including advanced marital age, higher levels of postgraduate education, and the changing role for women in society. This is reflected in the findings that from 1993 to 2003, the number of new fathers >35 years increased by 15%.[1]

To date, the effects of aging on reproduction have largely focused on females. Advanced maternal age has traditionally been considered to be 35 years or older. Well-studied conclusions on infertility and birth defects exist with clear physiological upper limits for childbearing occurring with the onset of menopause. There are thus well-established standards with respect to the effects of aging on female reproduction. For example, female fecundity decreases gradually, but significantly, commencing at age 32 years. It then declines dramatically after the age of 37 years.[2] The reasons for this fertility decline are multifactorial with the total number of oocytes decreasing with age, partially owing to the process of atresia, yielding ~500 000 oocytes at puberty and then declining to ~25 000 at 37 years.[2,3] The current American Society of Reproductive Medicine guidelines recommend expedited evaluation and treatment of failed conception following 6 months in women older than 35 years and immediately in women >40 years of age.[4]

Recently, there has been an increased focus on the effects of aging in men. In their chapter, Conti and Eisenberg[5] present a comprehensive and timely summary of the risks associated with advanced paternal age (APA). The authors discuss the difficulty in delineating the absolute effects of APA on fertility, since the majority of studies simply do not account for it. Numerous studies have examined the components of the semen analysis and found decreasing volumes, motility, morphology, and concurrent increases in DNA fragmentation;[6] however, these changes could still allow conception with relative ease. The same does not occur in females, since once their reproductive cycle is completed, fertility becomes impossible. Furthermore, with the increasing availability of assisted reproductive technologies (ARTs), simple declines in semen analysis, or even remote vasectomy, are obstacles that are simple to overcome.

There is currently no clear consensus for the definition of APA, which makes a meaningful clinical discussion challenging and analysis of previous data very difficult. Many studies typically define APA as 35–50 years of age, whereas others have taken to stratifying APA into 5-year brackets.[7] One could argue that moving forward, research on male fertility should include some type of breakdown of the data into male age subpopulations. Counseling regarding the risks of APA should still be conducted with all couples. Conti and Eisenberg[5] nicely highlight the increased relative risks of autism, schizophrenia and bipolar disease in APA; however, the absolute risks remain quite low. Nevertheless, Andrologists should develop a personal response to questions that patients will have about cryopreservation at a younger age to prevent the negative effects of aging. Given that there are published reports of successful pregnancies following sperm cryopreservation of up to 28 years,[8] the practice of freezing one's sperm at a younger age will no doubt be getting further attention in the future.

REFERENCES

1 Bray I, Gunnell D, Davey Smith G. Advanced paternal age: how old is too old? *J Epidemiol Community Health* 2006; 60: 851–3.
2 Baker TG. A quantitative and cytological study of germ cells in human ovaries. *Proc R Soc Lond B Biol Sci* 1963; 158: 417–33.
3 Broekmans FJ, Kwee J, Hendriks DJ, Mol BW, Lambalk CB. A systematic review of tests predicting ovarian reserve and IVF outcome. *Hum Reprod Update* 2006; 12: 685–718.
4 American College of Obstetricians and Gynecologists Committee on Gynecologic Practice; Practice Committee of the American Society for Reproductive Medicine. Female age-related fertility decline. Committee Opinion No. 589. *Obstet Gynecol* 2014; 123: 719–21.
5 Conti SL, Eisenberg ML. Paternal aging and increased risk of congenital disease, psychiatric disorders, and cancer. *Asian J Androl* 2016; 18: 420–4. [Doi: 10.4103/1008-682X.175097] [Epub ahead of print].
6 Johnson SL, Dunleavy J, Gemmell NJ, Nakagawa S. Consistent age-dependent declines in human semen quality: a systematic review and meta-analysis. *Ageing Res Rev* 2015; 19: 22–33.
7 Ramasamy R, Chiba K, Butler P, Lamb DJ. Male biological clock: a critical analysis of advanced paternal age. *Fertil Steril* 2015; 103: 1402–6.
8 Feldschuh J, Brassel J, Durso N, Levine A. Successful sperm storage for 28 years. *Fertil Steril* 2005; 84: 1016–7.

[1]McMaster Institute of Urology, Hamilton, ON, Canada; [2]Scott Department of Urology, Baylor College of Medicine, Houston, Texas 77030, USA; [3]Men's Health Center, 8240 Naab Road, Suite 220, Indianapolis, Indiana 46260, USA.
Correspondence: Dr. JR Kovac (jkovac@urologyin.com)