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Delaying Pregnancy

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Natural menopause occurs around the mean age of 50 [1-3]; however, within the past few years, timelines associated with family planning have changed dramatically. Modern societies have demanded for more options to extend the female reproductive lifespan improving the odds of conceiving at a later age, but is this right and/or ethical? What does the future hold?

It is well established that female reproductive performance dramatically drops around age 40 [4] due to the reduction of the ovarian reserve (i.e. the pool of quiescent follicles); however, increasingly more women are seeking to procreate beyond the capacity of their innate biological clocks. Technological advancements in assisted reproduction have made this a possibility.

Starting a family later in life is not always a matter of choice. In fact, infertility often forces patients to attempt *in vitro* fertilization (IVF), a procedure that may take time to be successful. Cancer is yet another example where afflicted young women are forced to delay starting a family, while preserving their capacity of future fertility. On the other hand many women are choosing to conceive later in age. We reside in a rapidly evolving society and many of the decisions involved with the responsibilities of parenthood are more heavily influenced than what would have been decades ago. Today, socio-economic factors play pivotal roles on influencing a young woman's decision to delay starting a family. US statistics have reported that from 1973 to 2009, the birth rate for women in their 20s has declined steadily over the last two decades, while increasing for women in their 30s [4]. A similar increase is seen for women in their 40s perhaps suggesting changes in personal and professional priorities for women of younger ages. Notably, the birth rate for women in their 50s depicts a remarkable 300 percent increase since 1997, the year when data for women age 50 and over first became available.

It has been proposed that the increasing trend in birth rate for women over 35 within the last 20 years could be due to the practice of assisted reproduction techniques [5], however, IVF success rates have been noted to decline after age 40 [6] due to the reduced developmental potential of ovarian follicles. Alternatively, egg donation programs offer a solution to this problem, but continue to be topic of much controversy. Specifically, many ethical concerns involving the safety of the procedure, the health (both short and long term) of donors and offspring and the existence of financial retribution for such donations still need to be resolved.

Studies are currently investigating new alternatives for prolonging reproductive lifespan. As previously mentioned, menopause ensues when the ovarian reserve is nearly exhausted around 50 years of age [7]. However, there are conditions, such as premature ovarian failure (POF), when this event occurs before the age of 40 [8]. Slowing down the process of follicle recruitment and by doing so preserving the population of quiescent follicles could result in the extension of female fertility. POF patients or women seeking to reproduce later in life may indeed benefit from such applications. Another possibility for the extension of reproductive life relies on the production of oocytes from somatic cells. In this scenario, the nucleus of an adult somatic cell would be injected into an enucleated oocyte. This oocyte could even be generated *in vitro* from embryonic stem cells (ESC) or induced pluripotent stem cells (iPS). This technique coupled with the haploidization of the somatic cell and the successful production of an embryo may sound a bit sci-fi, but the field is currently in full swing [9,10].

One thing is clear, it is not difficult to imagine the ethical implications of all this. Once proven effective, these technologies will only add more fuel to the fire. Many are already opposed to the use of IVF for women over 40 due to the potential of serious health risks for the mother-to-be [11]. Yet the fact of the matter remains; a growing number of women are choosing to conceive later in life.

In any case, the risk-benefit analysis needs to be well assessed in order to ensure safety and efficacy for both the women and their future offspring. Risks for gestational diabetes, hypertension and premature birth increase with age and women with late menopause are more likely to be affected by breast cancer, posing a possible limitation to fertility extension applications. On the other hand, risks for genetic abnormalities and autism in offspring correlate with the age of the mother and scarce are the data on long-term consequences. In the end, precise information, risk assessment and clinical management will be the key for an effective decision process. Safe technologies that fulfill the desire of a mother having a child later in age are welcomed, but physicians, scientists and policy makers still have to come to a general agreement that will not only meet patient's needs, but also preserve and promote their overall wellbeing. And let us not forget that some of these patients will be tomorrow's generations.

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