

The Impact of Elective Egg Freezing Technology

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Abstract

Advancing maternal age, especially after the age of 35, is associated with a continual decline in fertility potential. Recently, sophisticated techniques have been refined that make cryopreservation (freezing) of oocytes (eggs) a safe and efficacious method of pursuing fertility preservation in relatively young women. This technology has the potential to make a significant social impact by empowering women to have greater control over their reproductive future.

Keywords: Oocyte; Cryopreservation; Egg; Freezing; Fertility preservation

Capsule

Oocyte cryopreservation has the potential to make a significant social impact.

Recently, the technology used to freeze (cryopreserve) human eggs (oocytes) in the context of an *In Vitro* Fertilization (IVF) cycle has significantly advanced [1-3]. Consequently, many centers around the world have repeatedly demonstrated competence in oocyte cryopreservation with resulting pregnancies [1,2]. This success led to the 2012 decision by the American Society for Reproductive Medicine (ASRM) to remove the experimental label from oocyte cryopreservation [1]. To fully appreciate the potential impact oocyte cryopreservation may ultimately make, we must first consider the historical context of this advance and the possible applications for this technology moving forward.

Reproduction has been and will always be central to the human experience. For thousands of years there was essentially no mechanism other than abstinence with which human beings could control the timing of reproduction. This resulted in women undergoing childbearing relatively early in their lives. Many perceive this early childbearing to functionally conflict with career advancement for many women. The introduction of oral birth control pills as a form of contraception in the 1960's fundamentally altered this paradigm and afforded women for the first time the power to control their fertility and delay childbearing. As a result, the age at which women achieve pregnancy has continually and significantly increased since the 1960's, especially in wealthy nations.

Unfortunately, fertility potential in women decreases with age; especially after the age of 35. Many women who would be mildly sub fertile in their 20's are unable to achieve pregnancy via natural intercourse alone in their mid-late 30's and early 40's [1,2]. Consequently, the utilization of assisted reproductive technologies such as *In Vitro* Fertilization (IVF) to achieve pregnancy is relatively common in this age group. However, even with such measures, pregnancy rates are low, generally not exceeding 10% per IVF attempt, after the age of 40. Therefore for many women, delaying childbearing until their late 30's or early 40's results in a significantly lower possibility for achieving pregnancy with their genetic child.

The first pregnancies resulting from cryopreserved oocytes and embryos were reported in the mid 1980's [1,4]. While pregnancy rates associate with embryo cryopreservation were encouraging, survival rates of cryopreserved oocytes was exceptionally poor [5]. Therefore, for the past several decades, a solution to minimize the effect of maternal age on fertility decline has been to undergo an IVF cycle, cryopreserve embryos, and place these embryos into the uterus at the time pregnancy is desired. Because fertility for the most part is felt to

be tied to ovarian age, rather than the age of the uterus, pregnancy rates using this approach were encouraging.

A central limitation of embryo cryopreservation, however, is that this approach requires women to choose a male sperm donor to fertilize an oocyte (egg) prior to cryopreservation. Early attempts to freeze unfertilized oocytes were generally discouraging and not felt to be a viable option for fertility preservation [5]. While embryo cryopreservation did offer a viable option for fertility preservation in some couples, this option was unappealing for some women who did not have a male partner at the time of desired fertility preservation. Until recently, cryopreservation of embryos was accomplished with a technology known as "slow freezing." This has been replaced with a more sophisticated technology known as "vitrification" which is generally felt to be a superior technology for the cryopreservation of embryos.

Following the success of vitrification investigators began to explore the feasibility of applying vitrification to unfertilized oocytes. Subsequently major centers in the United States and in Europe began to demonstrate concrete success in achieving pregnancies using embryos that were derived from unfertilized oocytes that had been cryopreserved using vitrification, thawed, fertilized with sperm, and then transferred in to the uterus. These initial reports led to dozens of centers, including ours, demonstrating the ability to achieve pregnancies following the cryopreservation of unfertilized oocytes. Currently, pregnancy success rates from IVF cycles using oocytes cryopreservation are comparable to fresh IVF cycles; a feat that has only been realized in the past several years [1,2,6-9].

The ability to efficiently and effectively cryopreserve oocytes has the potential to have a mammoth social impact over the next several decades. Prior to this technology, women entering their mid to late 30's electing to defer pregnancy, accepting a continually declining age related fertility potential and the possibility of not ever having their own genetic child. Oocyte cryopreservation empowers women to delay childbearing without committing, at the time of the procedure, to what

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sperm will be ultimately used for fertilization. Some have compared the ultimate social impact of oocyte cryopreservation to the introduction of birth control pills. Oocyte cryopreservation also has other applications. This technology is likely to emerge as a central tool for preserving fertility in young oncology patients who have not initiated or completed childbearing. Additionally, couples undergoing IVF who have ethical or moral objections to cryopreserving embryos may avoid this concern with oocyte freezing.

Leading centers around the world, including ours, now routinely offer oocyte cryopreservation for fertility preservation. Over the past several years, oocyte cryopreservation has become increasingly visible in the public eye. High profile celebrities such as Kim Kardashian have recently pursued oocyte cryopreservation for fertility preservation. Oocyte cryopreservation is recommended for all young women wishing to maximize their future fertility.

Because the sharpest decline in a women's fertility occurs after the age of 35, oocyte cryopreservation is most effective if pursued at a relatively young age; ideally before the age of 30 [1]. In healthy women, it is believed that the average chance of achieving a pregnancy from one mature egg is approximately 10-12% [8]. Therefore, on average, freezing 10-12 or so mature eggs from a young woman generally provides a good statistical chance for achieving pregnancy up to their late 40's. Ultimate pregnancy rates resulting from oocyte cryopreservation are known to reduce most sharply after the age of 38 [10]. While obtaining this number of eggs is common in young women, some women may require multiple IVF stimulation cycles to "bank" this number of oocytes. Therefore, oocyte cryopreservation cannot ensure future fertility. Rather, this strategy serves as an "insurance policy" that could be employed if pregnancy with natural intercourse is not achieved at the desired time in the future. Women interested in

oocyte cryopreservation are encouraged to discuss the capabilities and limitations of the procedure with a physician specializing in assisted reproductive technologies.

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