

# Stopping the Biological Clock – Who Benefits?

## Abstract:

Eternal youth is here, at least for the females. This is what tabloids are trumpeting. The ability to store oocytes in order to prevent age-related fertility decline is being widely promoted in Ireland and worldwide, by both fertility clinics and the lay press. This service is referred to as ‘social oocyte freezing’ and is subject to significant medical, ethical, lawful and financial implications for both patients and assisted reproduction clinics performing the service. It is imperative that medical professionals suggesting ‘social oocyte freezing’ to their patients are able to provide detailed and accurate information, in order for an informed decision to be made. This review will detail the arguments for and against ‘social oocyte freezing’ and discuss the ethical and financial considerations for this controversial service.

Over the past decade the field of assisted reproductive technology (ART) has greatly advanced in the area of fertility preservation due to the push for a service for women and men with a malignant disease. Such patients face the risk of becoming infertile as a side effect of the gonadotoxic treatment they receive. The development of vitrification (‘snap freezing’) has revolutionised oocyte cryopreservation, leading to greater oocyte survival post-thaw and the potential for increased pregnancy rates<sup>1,2</sup>. However, in recent times, oocyte cryopreservation or ‘oocyte freezing’ is gaining considerable interest as a potential option for fertility preservation in women who wish to postpone childbearing for different reasons. Reproductive aging in females starts before they are born. The number of oocytes has reduced from 7 million in utero to 2 million at birth. This irreversible process creates a defined timeline for reproduction in females. Women are at the peak of their reproductive potential when they are in their twenties, with reproductive aging beginning when the woman reaches 30 years of age, resulting in decreased pregnancy rates and increased miscarriage rates. After the age of 43 years, the chances of a woman becoming pregnant naturally or artificially are extremely reduced. Therefore, while the ideal age for ‘social oocyte freezing’ to be performed is when women are in their 20s, in reality, it is mostly performed after the age of 35<sup>1,2</sup>. Combining a career and motherhood at the same time is a challenge for many women today. ‘Social oocyte freezing’ offers hope to women who wish to have children later in life, but at what cost?

As women age, the quality and quantity of oocytes they produce dramatically decline, with the incidence of chromosomal abnormalities in oocytes increasing exponentially. This often leads to aneuploidy or a genetically abnormal embryo upon fertilization resulting in decreased pregnancy rates, increased miscarriage rates and increased neonatal genetic disorders<sup>3</sup>. Social oocyte freezing offers an option for women to preserve their own oocytes at the prime of their reproductive ability. This could potentially make high quality ‘young’ oocytes available to the woman later in her life. This would negate the need for egg/embryo donation and avoid the legal ambiguity surrounding such interventions. The probability of achieving a pregnancy following oocyte freezing (vitrification) is between 5-10% per oocyte thawed, depending on the age of the woman and the number of oocytes collected<sup>4</sup>. Oocyte freezing, while technically very successful, remains to be proven in terms of pregnancy. As a medical intervention social oocyte freezing has its inherent risks. All patients need to undergo hormonal stimulation, with ovarian hyperstimulation syndrome (OHSS, approximately 1%) and surgical complications, such as infection, bleeding, bowel injury at oocyte collection a reality (approximately 1/1000).

As regards children born after ART there is an associated elevated risk of preterm birth and an increased genetic malformation rate in children born from the technology<sup>5</sup>. In general, the risks associated with ART are relatively low and in the case of infertility, considered acceptable by most couples and medical professionals. However, due to the lack of long-term follow up studies of children born from such interventions, there are still many unknowns. One consideration is the potential risk of epigenetic changes and imprinting defects following oocyte cryopreservation and in vitro culture of embryos<sup>6,7</sup>. The quality of oocytes should be unaffected by the duration of storage as these cells are in a ‘glass like’ state. Yet, prolonged contact with the solutions they are frozen in has not been fully investigated.

Pregnancy at an advanced maternal age is also associated with increased maternal and neonatal risks including: hypertension, preeclampsia, gestational diabetes, placenta praevia, placental abruption, caesarean section, genomic disorders, premature birth, low foetal birth weight and neonatal morbidity<sup>8</sup>. The challenges of a newborn arrival in late adulthood must not be ignored, particularly if pregnancy is postponed in the late forties and early fifties. While the reproductive clock has been stopped, the biological one has irreversibly progressed and evidence suggests that majority of ‘old mothers’ regret their decision to have a child so late in life<sup>9,10</sup>. Additionally, children born via oocyte freezing may be faced with taking care of their aging parents from a young age. The social and economic implications of aged-parental care on children and young-adults need also be considered when contemplating having children later in life. The potential associated risks to both mother and child, coupled with the low success rates per oocyte, need to be considered by fertile women thinking of undergoing social oocyte freezing to preserve their fertility. Oocyte cryopreservation can be an expensive procedure, and in Ireland, social oocyte freezing is paid for entirely by the woman/couple. In Ireland, the cost of only one cycle of ovarian stimulation with oocyte pick-up costs between 3,000 and 5,000. In most cases, several stimulation cycles are necessary in order to achieve oocyte numbers to give a positive chance of pregnancy. In addition to this price, annual storage costs have to be added. Finally, there is the additional cost of having, potentially several, thawing-transfer cycles (including fertilization with the partner’s sperm) which cost approximately 1,000 per cycle.

The ‘commercialization of reproduction’ raises many ethical issues. With the clinics providing such treatments benefiting from this emerging market, the American Society of Reproductive Medicine (ASRM) has warned about ‘giving patients false hope’<sup>11</sup>. In instances where social oocyte freezing is funded through government or company health insurance programs it is extremely necessary that the women undergoing the treatment fully understand the risks associated and the potential failure rates. One concern is providing false hope to women who delay having children at a young, fertile age only to undergo unsuccessful ART treatment using their frozen oocytes later in life. In Israel<sup>12</sup>, women between 30 to 41 years of age are able to undergo four oocyte-retrieval cycles funded by Israeli health funds<sup>13</sup>. These oocytes can be fertilized and transferred back to the woman up to 54 years of age. While ART makes it possible for women to get pregnant at an advanced age, it is important to consider the severe health risks associated with such a pregnancy. Additionally, the ability to care for a child or teenager at ages over 60 is a challenge and the ethics of such medical interventions need to be carefully considered.

Although social oocyte freezing does not solve the underlying problem of marrying a career with motherhood for women, it may be beneficial in specific situations. Informing patients of the potential health risks to themselves and the future child, the unknown long-term outcome of ART children and the relatively new technique of vitrification, in addition to the financial and psychological strain, are critical. Medical professionals proposing social oocyte freezing to their patients, should be up-to-date with all the above mentioned data. In addition, long-term follow-up studies on children born following social oocyte freezing programs are imperative. The large number of oocytes needed, in addition to the risks associated with ovarian stimulation and oocyte collection may deter women from availing of social oocyte freezing as a ‘back-up plan’ for their future fertility.

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