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EGG CRYOPRESERVATION: AN UPDATE ON AN EMERGING REPRODUCTIVE TECHNOLOGY

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Egg cryopreservation or freezing is a technique that was first demonstrated to be a success in the mid-1980s with the first report of a live birth from frozen and thawed human eggs. This technique, however, was abandoned as a routine clinical option after initial concerns that egg cryopreservation led to an increase in chromosomal abnormalities[1] and as the transfer of cryopreserved embryos became more commonplace. Interest in this technique has been recently renewed as a means of preserving the eggs of women about to undergo chemotherapy and for patients who object to embryo cryopreservation on religious or moral grounds. In particular, this procedure is being investigated as an alternative to embryo cryopreservation by countries that do not permit the freezing of embryos, such as Italy and Germany, in addition to fertility centers in the U.S., which recognize both a need and the financial incentive for offering this technique. It has been calculated that 936 children worldwide have been born from cryopreserved eggs as of April 2009.[2]

TECHNICAL HURDLES AND SCIENTIFIC PROGRESS

The egg (oocyte) is the largest cell in the human body and has a high water composition. This water must be replaced by a cryoprotectant to prevent the formation of ice, which is damaging to the cell. This can be difficult as the egg membrane in a mature, fully formed egg cell is generally impermeable to cryoprotectants. One potential solution to this obstacle is to preserve less mature egg cells (germinal vesicle stage), which have increased membrane permeability and lower rates of abnormalities resulting from the freezing process, although these must undergo the additional step of *in vitro* maturation prior to fertilization.[3] Two cryopreservation methods are currently being used, a slow freeze/rapid thaw method and vitrification, a newer "flash freeze" method. While clinical studies are needed to determine which method is more successful, the number of live births from vitrified eggs is fast approaching the number of births from slow frozen eggs, even though the first vitrification birth occurred 13 years later than the first slow-freeze birth.[4] Cryopreserved eggs are difficult to fertilize due to a hardening of the zona pellucida (membrane around the egg). Because of this, cryopreserved eggs must be fertilized by intracytoplasmic sperm injection.

The rates of post-thaw egg survival, fertilization, and live births have varied from study to study, although additional refining of the methods used for cryopreservation have greatly improved success rates. This has led Dr. Michael Tucker, Scientific Director of Georgia Reproductive Specialists, to state

> After fifteen years of investigating the potential for routine clinical application of human oocyte cryopreservation, I can safely say that this process has now come of age. In spite of the vagaries of reproductive biology and the inherent variability in gamete quality between individuals and the embryos arising from different couples, a problem that we constantly wrestle with in assisted reproduction, we are now in a position to achieve a leveling of the reproductive playing field such that oocytes as well as sperm and embryos can now be cryopreserved at a comparable rate of survival. This has been largely due to the consistency brought to gamete and embryo cryostorage utilizing vitrification technology.[5]

HEALTH CONCERNS

Oocyte cryopreservation is considered to be an experimental procedure by the American Society for Reproductive Medicine given the lack of studies determining the safety of this procedure to the resulting children.[6] A recent literature review of egg cryopreservation studies concluded from their analysis that children born from egg cryopreservation are not placed at an increased risk for congenital abnormalities in comparison to naturally conceived children, although additional study is needed.[7] An additional health concern is the increased risk of Ovarian Hyperstimulation Syndrome to women given the large amounts of fertility medications needed to collect a sufficient amount of eggs for cryopreservation and subsequent *in vitro* fertilization cycles.[8]

ETHICAL CONCERNS

Aside from traditional concerns of the exploitation of women through egg harvesting, a primary ethical concern associated with the cryopreservation of eggs is its marketing and use to electively delay childbearing, potentially past reproductive age. It has also been proposed that cryopreserved eggs be banked for donation as success rates improve. This is morally problematic for many from a Christian worldview as such eggs are intended for use outside of the marital relationship or as a means of treating infertility within a marriage which would effectively introduce a "third party" into the relationship. Positively, the cryopreservation of eggs is predicted to lead to a decrease in the number of surplus embryos in cryostorage by shifting current practice away from the cryopreservation of surplus embryos towards the cryopreservation of eggs. This will eliminate what has become for many the difficult dilemma of deciding the fate of surplus embryos after their family is complete.

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[1] Jeffrey Boldt, Donald Cline, and David McLaughlin, "Human Oocyte Cryopreservation as an Adjunct to IVF-Embryo Transfer Cycles," *Human Reproduction* 18 (2003): 1250.

[2] N. Noyes, E. Porcu, and A. Borini, "Over 900 Oocyte Cryopreservation Babies Born with No Apparent Increase in Congenital Anomalies," *Reproductive BioMedicine* 18 (2009): 769-776.

[3] Tao Tao and Alfonso Del Valle, "Human Oocyte and Ovarian Tissue Cryopreservation and Its Application," *Journal of Assisted Reproduction and Genetics* 25 (2008): 289.

[4] Noyes et al., 770.

[5] Michael Tucker, PhD, email message to author, October 8, 2009.

[6] Practice Committee of the American Society of Reproductive Medicine, "Ovarian Tissue and Oocyte Cryopreservation," *Fertility and Sterility* 90 (2008): S241-S246.

[7] Noyes et al., 773-774.

[8] Because of this, most female cancer patients are not considered to be candidates for oocyte cryopreservation due to the potential negative effects of estrogen on the primary tumor (Practice Committee of the American Society of Reproductive Medicine, S241).