

What's a Young Woman to Do?

The Pros and Cons of Social Egg Freezing

BY JOANN PALEY GALST, PhD
CHAIR, THE AFA MENTAL HEALTH ADVISORY COUNCIL

Many modern women postpone childbearing in order to complete their education, get their career on solid footing, or find the right partner with whom they want to share their life.

As a result, increasing numbers of women find themselves over age 35 and confronting fertility challenges. Improvements in oocyte cryopreservation (i.e., egg freezing) offer women the possibility of greater control of their reproductive future by potentially extending their fertility. While women with a history of premature ovarian insufficiency, ovarian cysts, living in an area with high exposure to pesticides or heavy metals, or undergoing exposure to chemical or biological warfare due to military service may also consider egg freezing, the largest numbers of women considering social egg freezing are likely to be those who either desire or foresee delaying their childbearing years.

The Female Facts

While the ovaries of a 20 week old female fetus contain 4-7 million oocytes, this is halved by birth, and by puberty approximately 400,000 oocytes remain. Of these, only 400-500 will eventually undergo ovulation. Ultimately, a woman's ovarian reserve quantity decreases with advancing age, as does the quality of her oocytes (e.g., there is a higher incidence of chromosomal anomalies) which, in turn, reduces the

chances of successful fertilization, implantation, and early embryo development. By age 35, a woman has lost ~95% of her eggs and the rest are aging rapidly (Baker, 1963; Practice Committee of the American Society for Reproductive Medicine, 2006).

The Fertile Facts

Young women are often unaware of the early reduction of their fertility, declining with age from her mid to late 20's onward, most notably between 35 and 40 years and over. To understand this better, consider the fact that the proportion of women who fail to conceive after one year of trying increases from 5% in those under age 25 to 30% in those 35 and older, and the rate of spontaneous miscarriage increases from ~10% before age 30 to 34% at age 40, reaching 50-75% at ages above 45 (American Society for Reproductive Medicine, 2003; Dunson, Baird, & Colombo, 2004). With time, there are also increased opportunities to contract genital tract pathologies such as STIs, tubal damage, fibroids, endometriosis, etc., and these can interfere with fertility, implantation, and ultimately successful pregnancy.

Many women incorrectly believe that assisted reproductive technology can extend their fertile years. However, in vitro fertilization (IVF) is also increasingly unsuccessful with rising age (i.e., the chance of a live

birth through IVF is 41% for women under 35, 32% for ages 35-37, 22% for 38-40, 12% for 41-42, and 5% for ages 43-44; Centers for Disease Control and Prevention, 2009).

Fertility Trends

There is a trend for women to delay the time at which they give birth to their first child, rising in the U.S. from an average age of 21.4 in 1970 to 25.0 by 2006. Women between ages 30-34 are now the largest contributor to the total number of U.S. births, with the contribution of women over age 35 rising dramatically, as well (Martin, Hamilton, Sutton, et al., 2009; Mathews & Hamilton, 2002, 2009). However, in a 2001 study by from the Center for Work Life Policy, one third of high achieving 41-55 year old women were childless with only 14% of them being so by choice (Hewlett, Luce, Shiller, & Southwell, 2001).

Social Dimensions

Modern contraception has made the timing of having a baby more within an individual's choice. This and the women's movement encouraged women to aspire to further their education, strive for career advancement, and obtain both financial security and work stability for themselves, all of which have contributed to women postponing the age of starting to have their children. Nevertheless, biology still determines reproductive outcomes and even assisted reproductive techniques have not been able to change the fact that ages 20-35 remain the best age for women to reproduce in terms of physiology and the most favorable maternal and fetal outcomes while men still have a larger window of opportunity to reproduce with their own gametes. Thus, social realities and biological realities are currently out of sync for women in the U.S.

Egg freezing offers the potential for women to extend their biological time clock and delay childbearing for social or career reasons. It could become a fundamental tool of family planning, empowering women further with regards to their reproductive autonomy. But, should women have to freeze their eggs and delay motherhood until their 40's just so they can compete in a professional environment designed by and for men? This is a socio-political question and,

regardless of your answer, to change the climate of the U.S. workplace will require more women in positions of power and influence and that is still a long way off. Until then, if women want both professional advancement and motherhood, they will likely wonder if they should take advantage of what science has to offer them. The information presented below is an attempt to educate women regarding the process involved in egg freezing and offer a risk analysis paradigm to help with decision making.

What Process is Involved?

Egg freezing is neither an easy nor an inexpensive procedure. It starts out just like the technique to harvest eggs for IVF. A woman injects herself with hormones to stimulate multiple egg production. This requires serial blood sampling and transvaginal ultrasounds to monitor the process. When the eggs have reached an adequate size, with the woman under IV sedation, a reproductive endocrinologist uses a needle to extract the eggs from the ovaries before cryopreserving them (see below for information about the freezing process). When a woman is ready to use her eggs, they will need to be thawed and fertilized. Not all the eggs may survive the cryopreservation and thawing process. It is more difficult for eggs that have been frozen to be fertilized by sperm due to changes that occur in the egg's outer coating and thus intracytoplasmic sperm injection (ICSI), a process in which a single sperm is injected into the egg, is required. Not all of the eggs are likely to fertilize. For those that do fertilize, the process of embryo development will be observed within a lab at the fertility center, and some may not continue to develop. For those that survive, a certain number of embryos (depending on the woman's age at freezing the eggs as well as the quality of the embryos that have developed) will be transferred using a catheter that is threaded through the woman's cervix into her uterus. Not all, or perhaps none, of the transferred embryos will implant or continue to develop.

Eggs are the largest cell of the body and contain a large proportion of water. A major problem in freezing

eggs is the damage that can occur to the membrane as a result of the formation of ice crystals during the freezing process, potentially leading to the rupture of the cell membrane and causing cellular destruction. This was a particularly difficult obstacle to overcome with the original slow freezing method of cryopreservation. A newer technique called vitrification, or ultra rapid freezing of eggs, allows no time for cell-destroying ice crystals to form. Vitrification does require high cryoprotectant concentrations, however, to protect the cell from the stresses of freezing and thawing (Chang, Shapiro, Bernal, et al., 2008).

What are the Success Rates?

What percentage of frozen eggs can be expected to result in full-term pregnancies? This is perhaps the most important question to women and the one that is hardest to answer due to the lack of adequate data at present. We do know that for the best chance of success, a woman should be 35 years of age or younger when she freezes her eggs and should probably have around 20 eggs frozen to have a chance for one pregnancy with vitrified eggs. This would require, in all likelihood, going through several cycles of ovarian stimulation and egg retrieval.

Data from the 1990's until the early 2000's using slow freezing of eggs showed live birth rates of approximately 2-10% per embryo transferred. Recent, although scant, data for vitrified eggs suggests that approximately 85% of vitrified eggs will survive the thaw and a pregnancy rate of approximately 45% can be achieved per cycle in women who froze their eggs before age 36, although lower rates, i.e., between 13-39%, have also been reported, some of which were likely to have been in women who were older at the time of egg freezing (Borini, Levi Setti, Anserini, et al., 2010; Cobo & Diaz, 2011; Cobo, Kuwayama, & Perez, 2008; Oktay, Cil, & Bang, 2006; Rienzi, Romano, Albricci, et al., 2010; Ubaldi, Anniballo, Romano, et al. 2010).

It is important for women to understand that even having eggs frozen before they are 36 years of age is

NO GUARANTY they will thaw successfully, fertilize successfully, implant successfully or result in an ongoing pregnancy with a live birth. A woman's best chance of having a child is still through timely and natural conception. Also, it is important for women to recognize that most women will never use their frozen eggs, as they will find a partner prior to needing to turn to their frozen eggs.

How Long Can Cryopreserved Eggs be Stored?

Current practice is that eggs can be stored approximately 10 years. However, eggs may be able to be frozen indefinitely. Egg cryopreservation has not been available long enough for experts to be certain at this time.

Safety:

For Women: At present, although long term risks of exposure to the high doses of hormones that are typically used during ovarian stimulation appear minimal, there remains a dearth of research. Many women, however, experience some pain and bloating and can feel intense emotions during stimulation. The potential risk of serious complications from ovarian stimulation and egg retrieval (e.g., ovarian hyperstimulation requiring hospitalization, intraperitoneal bleeding, ovarian torsion, ruptured ovarian cyst, infection) is low, i.e., less than 1%. The risk of minor complication needing medical attention (e.g., primarily ovarian hyperstimulation) is ~ 8.5% (The Practice Committee of the American Society for Reproductive Medicine, 2008). Becoming pregnant in one's 40's also carries with it a higher chance of complications, including developing preeclampsia, diabetes, and hypertension. However, if a woman is healthy to begin with, these risks are small (Cleary-Goldman, Malone, Vidaver, et al., 2005; Paulson, Boonstanfar, Saadat, et al., 2002).

For Babies that May be Created: Since only approximately 1500 babies have been born worldwide from cryopreserved eggs, the data is limited. Thus, definitive conclusions regarding either the efficacy or the safety of this procedure cannot be drawn at

present. Of the preliminary data that is currently available, the incidence of congenital anomalies was found to be no higher than for babies conceived naturally, nor were there any differences in median birth weight. However, no data was included on the number of pregnancies that were terminated because of fetal anomaly (Chian, Huang, Tan, et al., 2008). It should be noted that there is an increased risk of infertility and of transmitting genetic abnormalities to offspring when conceived using ICSI. This may be able to be averted if genetic testing is performed on the male partner/donor prior to using the sperm for fertilization (Kurinczuk, 2003;

The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology, 2008a).

Costs

For ovarian stimulation medications, tests, monitoring, egg retrieval, and fertilization of eggs, the costs at present tend to run between \$12,000 - \$20,000 per cycle, and women are likely to require several cycles to have the suggested number of eggs frozen to optimize the chance of success. Storage costs for the cryopreserved eggs are often included for the first year and then cost several hundred to ~ \$600 per year after that. Egg freezing for social reasons is not covered by insurance.

Is Cryopreservation of Eggs Being Done in the U.S.?

The first successful pregnancy from cryopreserved eggs occurred in 1986 (Chen, 1986). As of 2010, 51% of U.S. IVF clinics report offering oocyte cryopreservation, with 64% of those offering it electively to women for social reasons (36% offering it only to women about to undergo treatment for cancer or after IVF if the woman has a moral objection to embryo cryopreservation). Of the clinics offering this procedure, 87% accept patients up to 37 years of age, 49% accept patients up to 40 years of age, and only 26% accept women beyond 40 years of age for cryopreservation of their eggs (Rudick,

Opper, Paulson, et al., 2010).

What are the Ethical Issues One May Need to Consider?

-When is one too old to have a baby?

-What effect would deferral of childbearing with egg freezing have on society if it becomes common?

-Will the availability of this technique increase anxiety for young women concerned about their future fertility or empower women, allowing them to postpone childbearing for a longer period of time, just as men have been able to do.

-Egg freezing circumvents moral and ethical dilemmas for some who take issue with embryo freezing as they view the embryo as representing the beginning of life with all the rights offered to a person. Eggs that have not been fertilized do not have the capacity to develop into an embryo unless they are exposed to sperm.

Professional Guidelines

The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology (2008b) still categorize egg freezing as an experimental procedure that should not be offered or marketed as a way to defer natural reproductive aging and should only be performed under investigational protocol under the auspices of an institutional review board. It is recommended that oocyte cryopreservation patients meet with a qualified mental health professional for psycho-educational purposes to facilitate informed decision making regarding freezing oocytes and to understand the potential psychosocial implications of this choice.

The Decision-Making Process for Egg Cryopreservation for Social Reasons

As in making any other important decision, an individual needs to be fully and accurately informed of the risks and benefits of any medical procedure they are considering undertaking. The information above will hopefully help inform you. Table I offers pros and cons for you to consider in your own risk analysis.

Questions for Women to Ask

In an article entitled, Essential elements of informed consent for elective oocyte cryopreservation: A Practice Committee opinion, the Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology have recommended 13 points including information about the ovarian stimulation, retrieval, freezing, and the fertilization process as well as the fees and clinic-specific procedures and risks involved that a woman needs to know in order to make decisions and give informed consent to undergo oocyte cryopreservation. These can be found online at www.asrm.org/publications/detail.aspx?id=3988. This information will likely be offered to you by your reproductive endocrinologist. If not, ask, in order for you to be able to make an informed decision regarding freezing your eggs for nonmedical reasons.

In addition, you may want to ask the following questions as they relate to your own unique circumstances:

- If I freeze my eggs, what are my chances of taking home a baby?
- How many eggs do you recommend I freeze to have the best chance of taking home a baby?

Conclusions

Both sociological trends that encourage women to pursue higher education and enter the work force in significant ways and the inflexibility of the U.S. workplace tacitly encourage women to push the boundaries of their fertility. Reproductive technology is becoming more readily available to assist young women with this dilemma.

Young women have recently been advised to get HPV vaccines. Should it also be recommended that they freeze their eggs? Is it premature to apply this novel technique before its safety and efficacy has been reasonably established?

Oocyte cryopreservation is an evolving technology that remains considered experimental by the professional organization representing reproductive endocrinologists, yet over one third of U.S. fertility clinics offer egg freezing for social reasons. Egg freezing does not address important workplace issues that can support women in their desire to simultaneously combine work and motherhood (e.g., flexibility in work hours, allowance for family crisis without financial penalty, affordable childcare). Important questions still need to be answered before it would be recommended that all young women jump on the egg freezing bandwagon. Nevertheless, the technology does have the potential to change society. If adequate data demonstrate its efficacy and safety, it may empower women with regards to their fertility potential, giving them further control over reproduction and reducing gender inequities regarding reproduction.

There is a risk that egg freezing will come to be seen as "egg-surance" (Gracia, 2009), however, viewed as a preventive measure to be taken against future age-related sub-fertility in women., Marketing has the potential to play on women's fears and provide them with a false sense of security. The technology and its marketing have the potential to lead women to view egg banking as an equal alternative to having children naturally in their 20's or early 30's. But, there is no guarantee that it will work.

At present, there is not enough accumulated data for women to make truly informed judgments and derive conclusions as to whether this technique can meet their needs and expectations. As it stands now, oocyte cryopreservation offers a possibility, not a guarantee. Thus, caveat emptor. The best chance of having a baby still remains doing it naturally when you are under age 35. But, stay tuned. This is a technology on the rise.

Joann Paley Galst, Ph.D. is Co-director of Support Services and Chair of the Mental Health Advisory Council of the American Fertility Association and on the Board of Advisors of the Pregnancy Loss Support Program of the National Council of Jewish Women-NY Section. She is a psychologist in New York City specializing in

Table I. Risk Analysis for Social Egg Freezing

	PROS	CONS
SOCIOLOGICAL IMPLICATIONS	<p>May give women more control over their reproductive destiny</p> <p>Allows women to proactively maximize their chances of passing their own genes on to a child, regardless of age</p> <p>Gives women longer opportunity to complete education, advance careers, find suitable life partner, allow relationship to develop before biological time clock runs out</p> <p>Can help women avoid needing egg donation</p>	<p>No guarantee of successful pregnancy</p> <p>Unlikely most women will ever need to use their frozen eggs, yet accrue the cost of freezing</p> <p>Women may make important life decisions based on false assumptions that their fertility is safeguarded that wind up limiting their ability to become a mother in the future</p> <p>May give idea that childbearing can safely be postponed until even after age 40</p> <p>May encourage women to delay marriage</p> <p>May increase number of older parents</p>
PHYSICAL RISKS TO WOMAN	<p>Low</p>	<p>Risks are present (see safety section above)</p> <p>Requires medical procedures to be performed on healthy woman</p>
TO CHILD	<p>Thus far does not appear elevated beyond that in IVF with fresh eggs</p>	<p>As in any pregnancy, there is some risk (~3% overall) of congenital anomaly.</p> <p>Male children born from ICSI have higher levels of infertility & genetic abnormalities</p> <p>Risks involved in having an older parent</p>
PSYCHOLOGICAL RISKS	<p>Women are capable of determining their own willingness to accept risks</p>	<p>A false sense of security (having frozen her eggs, a woman may delay having children expecting success with these, yet may have poor results after thawing or fertilization & embryo development)-the thawing process may not work, not all survivors will be successfully fertilized, not all fertilized eggs turn into good embryos, not all good embryos implant and begin to grow within the woman's uterus.</p> <p>Women may feel pressured to prophylactically store their oocytes</p> <p>A woman may have a negative reaction after freezing her eggs as the process may lead to her confronting the reality of her life</p> <p>A woman may feel disappointed when she realizes that egg freezing offers no guarantee of a future pregnancy</p>
SUCCESS RATES	<p>Rates increasing as technology improves</p>	<p>Inadequate data at present to properly inform women of chances for success. No age-stratified outcome data yet, so no logical basis to predict success for women expressing interest</p>
AGE	<p>Young eggs have a better genetic competency</p>	<p>At present, if a woman freezes her eggs at 25 & plans to use them at 35, she may have a significantly higher likelihood of conceiving by IVF with her own fresh eggs than eggs frozen a decade earlier</p>
FUTURE FERTILITY	<p>Frozen eggs may possibly extend age at which women can bear their own genetic child</p>	<p>Unknown if egg freezing has an effect on future natural fertility</p>
SOCIO-POLITICAL IMPLICATIONS	<p>Empowering to women, offering greater reproductive freedom</p>	<p>May allow society to ignore problems in workplace that lead to women having babies later in life & not address the need for societal support for working mothers</p> <p>May further add to the commercialization of the fertility field, especially before randomized & long-term studies offer solid data on efficacy & safety for both women & children created</p> <p>Potential for manipulative, dishonest marketing</p>
UNUSED EGGS	<p>Less of a moral dilemma than frozen embryos but women should make disposition arrangements in case they do not need to use their eggs or they should die</p>	<p>Many unused eggs may be left behind as most women will never need to use their cryopreserved eggs</p>
STORAGE FACILITY	<p>Many IVF centers now offer cryopreservation of oocytes to single women for social reasons</p>	<p>The facility in which you froze our oocytes may cease operation requiring transfer of cryopreserved oocytes to another storage facility</p> <p>Cryopreserved oocytes may be lost as a result of a lab accident or events beyond the control of the storage facility.</p>

reproductive health issues including infertility and pregnancy loss and a past chair of the Mental Health Professional Group of the American Society for Reproductive Medicine. She has written extensively in the fertility field and is a co-author with Judith Horowitz and Nanette Elster of the recently published book entitled, *Ethical Dilemmas in Fertility Counseling*. She can be reached at 212-759-2783 or jgalst@aol.com, <http://www.wmhcnyc.org/galst/>

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