Egg freezing, procreative liberty, and ICSI: the double standards confronting elective self-donation of oocytes

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The consensus view among relevant professional societies opposing the offering of elective oocyte cryopreservation for potential future self-donation withstands neither clinical nor ethical scrutiny. The favorable risk-benefit ratio of this technology mandates both the prioritization of patient autonomy for informed women seeking to maximize—not guarantee—their chances of having genetically related children, and a justification for viewing egg freezing differently from intracytoplasmic sperm injection. (Fertil Steril® 2009;92:1509–12. ©2009 by American Society for Reproductive Medicine.)

Self-donation of oocytes offers promise as the twenty-first-century equivalent to the oral contraceptive. Its potential to "level the playing field" for women by permitting them time-unlimited control over their reproductive destiny has captured the public imagination and initiated widespread debate.

The well known age-related decline in fertility among women continues to present an often unyielding barrier to autologous procreation for many women who have delayed childbearing owing to personal or career considerations. These women, when fertility potential remains substantial, are most likely to undergo high-tech infertility therapies using their own eggs, often resulting in complicated pregnancies and multiple births. When fertility potential is poor, such women are often counseled to forego in vitro fertilization (IVF) with their own eggs, and to pursue donor oocytes obtained from young healthy women, an increasingly common practice that is clinically justified by the high success rates achieved. Nevertheless, these older recipients must sacrifice the desire to bear a genetically related child, a proposition that is personally or spiritually painful for many women.

Self-donation of oocytes has the potential to allow reproductively aging, informed, and determined women who have not yet met their life partner to proactively maximize their chances of passing their own genes on to a child, regardless of their age. Additionally, self-donation might appeal to women reluctant to pursue egg donation given their lingering perception that, despite widespread acceptability and ethical sanction, it potentially involves exploitation of the egg donor. Although the process of egg freezing via the traditional "slow-freeze" protocols has remained too inefficient to consider for the purpose of self-donation for future use, the recent advances in both slow-freeze technique and vitrification technology have enabled a dramatic improvement in the efficacy of oocyte cryopreservation (1, 2). For example, a 2008 study (3) comparing the performance of vitrified versus fresh oocytes demonstrated a reproductive performance of frozen-thawed eggs that was similar to fresh eggs. A vitrification survival rate of 97%, a fertilization rate of 76%, a clinical pregnancy rate of 65%, and an ongoing pregnancy rate of 48% were achieved.

Although confirmation of these results by other centers is awaited, these data clearly indicate that this is a technology that has arrived. Nevertheless, relevant professional societies, such as the American Society for Reproductive Medicine (ASRM), the American College of Obstetricians and Gynecologists, and the European Society of Human Reproduction and Embryology, appear excessively deliberate in adapting policies toward this inevitable technologic advance, and they have expressed an unqualified hesitancy reflecting a double standard regarding gender. More disturbingly, such opposition unjustifiably infringes upon the autonomy of appropriately informed women and—given the recent improvement in egg freezing efficacy—restricts what should be a legitimate offering in the beneficent management of age-related infertility. A reconsideration of the appropriate role of oocyte cryopreservation for elective fertility extension within the armamentarium of assisted reproduction is warranted.

Representing the consensus view among the American and European professional societies, the ASRM states: "Oocyte cryopreservation is not an established medical treatment. [It is] an experimental procedure that should not be offered or marketed as a means to defer reproductive aging, primarily

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because data relating to clinical outcomes are limited" (4). Clinical prudence and ethical practice dictate withholding sanction of novel technology pending evidence of efficacy and safety. However, marginalizing elective egg self-donation owing to its current clinical achievement ignores, in our opinion, a risk-benefit calculation that should legitimize this technology for appropriately informed women, and selectively imposes upon oocyte cryopreservation a burden of proof that has never been imposed on any advancement in reproductive technology to date, from IVF to intracytoplasmic sperm injection (ICSI).

In a recent study of the risks encountered by egg donors undergoing controlled ovarian hyperstimulation (COH) and ultrasound-guided transvaginal egg harvest—a scenario entailing identical risks to a patient seeking to freeze her own eggs—the rate of serious complication (ovarian hyperstimulation requiring hospitalization, intraperitoneal bleeding, torsion, ruptured ovarian cyst, or infection) was 0.7%, and the rate of minor complaints or complications necessitating medical attention (primarily ovarian hyperstimulation not requiring hospitalization) was 8.5% (5). Those reluctant to endorse the practice of elective oocyte cryopreservation based on safety considerations must justify why they think young egg donors, altruistic or entrepreneurial, may assert their prerogative to assume these small risks and undergo COH with oocyte retrieval, but women seeking to maximize their chances of autologous procreation should not do so. Moreover, a review of 200 births from vitrified oocytes showed no elevated incidence of congenital anomalies or low birth weight compared with IVF births from fresh oocytes (6). This constitutes more evidence of safety than was ever available before the early adoption of practices such as ICSI.

Indeed, the field of assisted reproduction in the United States has been criticized, perhaps justifiably, for repeatedly introducing, even promoting, laboratory breakthroughs into clinical practice without rigorous government-sponsored or supervised clinical trials to ensure safety and efficacy. Free-market dynamics combined with the disbanding of the Federal Ethics Advisory Board in 1980 and subsequent moratorium on federal sponsorship of IVF-related research or clinical endeavors have conspired to enable this unique evolution of assisted reproduction. The first American IVF baby was born in 1981, and just over a decade later, preimplantation genetic diagnosis was likewise imported from the United Kingdom without much testing for safety. Most dramatic was the leap of ICSI, an invasive and experimental technique, from a European fertility center to worldwide use, without what many would consider even cursory due diligence to establish its safety. And 15-plus years later, despite indisputable clinical efficacy, ICSI requires ongoing surveillance, because concerns persist regarding the genetic and epigenetic endowment of progeny derived from this procedure.

Given this history of rapid adoption of technology followed by concern and enhanced monitoring, the cautious stance by various organizations on elective egg freezing, while unprecedented, may well reflect a determination to better establish the safety of new techniques before their widespread use. Accordingly, some might argue, subjecting novel reproductive technology to institutional review board (IRB) oversight is both justifiable and prudent. We, however, disagree, and feel that the apparent assumptions underlying the current position that elective self-donation of oocytes is "experimental" and a comparison of the current—not just the past—disparity in how ICSI and elective egg freezing are viewed highlight a double standard that is sexist in effect, if not intent.

Our position derives from four specific arguments: First, novel technology should not be rendered "experimental" for the purposes of restricting its availability or mandating IRB oversight simply because its reported clinical efficacy is inferior to other techniques or remains below an arbitrarily chosen success-rate threshold. The proper place to address clinical efficacy disparities is within the informed consent process. Second, a newly adopted policy of closer scrutiny and stricter criteria to establish a novel technology as "safe" must be consistently applied. Third, the optimal way to enhance safety is by ASRM-sponsored registries with mandated reporting, not by reliance on local IRBs. And fourth, we should carefully differentiate the efforts by our professional society to formulate and strengthen practice guidelines from socioethical gate keeping—an endeavor fraught with controversy, given the often debatable merits of the underlying considerations, the infringement of procreative liberty that such gate keeping might entail, and the likelihood that as reasonable people continue to disagree over ethics, restrictive policies are frequently, and deservedly, reversed. Allow us to explain.

Analogous to other elective procedures, such as cosmetic surgery, egg freezing with subsequent live birth is no longer an oddity or isolated triumph. As it further establishes itself—a process that is continuous, not discrete—elective egg freezing will pass or fail clinical and ethical muster based on the rigor of its informed consent process, i.e.: Does the patient have realistic expectations of the risks, benefits, and alternatives? We feel that there is no basis to assume patients cannot understand that elective oocyte cryopreservation increases, but does not guarantee, their chance of autologous procreation. And this can be specifically assured by an ASRM-guided informed consent process, incorporating both literature-reported and center-specific success rates. Many may feel that the current relatively lower success rate of egg freezing renders it "experimental." We, however, seek a justification for the assessment of the risk-benefit ratio by ASRM and other bodies that have made judgments in this area superseding that of appropriately informed women who deem it beneficial, desirable, and justifiable to freeze their own eggs despite an expectation of less success. Informed consent to appropriately calibrate patient expectation, accordingly, negates the disparity in documented clinical success between the more established practices of ICSI or embryo cryopreservation and the newer technology of oocyte cryopreservation that is presumably being used to rationalize

elective egg freezing alone being "experimental" and requiring, consequently, IRB approval.

Alternatively, if safety remains the crucial factor motivating the singling out of egg freezing as "experimental" and in need of IRB oversight, we would object to both the absolute and relative merits of this determination. Novel as it is, egg freezing has established a notable record of reassuring preliminary data (6). Additionally, earlier lengthy experiences with sperm and embryo freezing have been benign and, arguably, augur well for a similar experience with egg freezing. This is in contrast to lingering questions about imprinting disorders and malformation attributable to ICSI which should raise the question as to why ICSI today should not be labeled "experimental" and subjected to greater IRB oversight of its safety implications.

Fairness demands consistency; yet, ultimately, we feel that neither egg freezing nor ICSI warrant the designation of "experimental" treatment. Just as informed consent addresses current clinical efficacy, an ASRM-sponsored national registry would best facilitate enhanced safety in assisted reproduction. This registry, with compliance and reporting mandatory for all programs listed by the Society for Assisted Reproductive Technology, could efficiently track all relevant pregnancy outcomes and thereby further illuminate questions of safety. Moreover, given the low risks of either egg freezing or ICSI, the likelihood that a local IRB will provide useful outcome detection seems to be remote. What is likelier, however, would be the infringement of procreative liberty by some of these IRBs as a consequence of their investigation of, and potential objection to, the propriety of widespread elective egg freezing.

And this invokes our final argument. The ASRM expresses opposition to the offering or marketing of egg freezing as "a means to defer reproductive aging, primarily because data relating to clinical outcomes are limited" (4). Primarily? What other factor(s) determined this opposition to elective egg freezing? Indeed, this phraseology leads us to suspect that what was found to be objectionable were the social implications of elective egg freezing. We acknowledge that widespread deferral of childbearing via egg freezing may transform society in unforeseen ways, akin to some of the unintended consequences, such as more sexually transmitted infection, wrought by the oral contraceptive and the sexual freedom it empowered. Nevertheless, we respectfully assert that ASRM should grant precedence to assertions of procreative liberty by women that present merely speculative, not tangible, danger.

Additionally, we are disturbed by the implied judgment that our society, having failed to sufficiently safeguard the ability of many women in their twenties and thirties to establish families without jeopardizing career advancement, cannot withstand the challenges posed by elective deferral of childbearing. Unlike their counterparts in many other countries, American women are bound to a relatively inflexible workplace that tacitly encourages them to push the bounds of their fertility. Indeed, many women who take the precaution of freezing their own eggs for future use may find a partner, conceive naturally, and never need their frozen eggs. For two reasons, this likelihood should not be considered to be a deterrent. First, men who undergo cancer chemotherapy and freeze sperm in advance wind up using their frozen specimens only ~4%–8% of the time (7), yet, all clinical guidelines recommend this procedure. Second, some women, despite awareness that their frozen eggs do not guarantee future autologous procreation, nevertheless derive benefit from the mere fact that their frozen eggs offer that possibility.

Finally, the larger debates looming over this discussion—how best should ASRM and other advisory bodies exercise their gate keeping roles when evaluating the ethical validity of new techniques and, furthermore, whether patients have been well served by the laissez faire nonregulation of assisted reproduction in the United States—can not be fully addressed in the constraints of this article. Suffice it to say that we do recognize both the difficulties encountered during ethical appraisal of various reproductive technologies and the appropriateness of opposing a specific technology when ethical liabilities clearly overwhelm the assertion of procreative liberty. However, we firmly believe that American patients have been well served by the absence of a regulatory agency, such as the British Human Fertilization and Embryology Authority, that has the legal capacity to prohibit reproductive technology pursuant to nonmedical misgivings. Indeed, ethical and social considerations against a reproductive technology must be carefully weighed against the prerogative of procreative liberty before they are used to curtail its use. And when reasonable people continue to legitimately disagree over the ethical merits and social repercussions of a particular reproductive technology, the presumption should be in favor of permissibility, given the great benefit that procreation is perceived to impart.

In summary, a cautious approach to elective self-donation of eggs is warranted; the potential for both societal transformation and manipulative, dishonest, and unseemly marketing remain great and have always been a challenge to patients and practitioners in this field. But for the informed woman seeking procreative liberty via greater control over her reproductive destiny, the considerations of autonomy and beneficence override those of commercialization, deleterious change and exploitation. The ASRM should reconsider its view on elective oocyte cryopreservation and support the clinically and ethically justified aspirations of single women seeking to maximize their likelihood of having genetically related offspring.

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