



## In defense of a regulated system of compensated egg donation for research

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### **Abstract**

Monetary compensation for human eggs used in research is a controversial issue and raises major concerns about women's health and rights, including the potential of exploitation and undue inducement. Human eggs are needed for various types of studies and without payment, it would be impossible to procure sufficient eggs for vital research. Therefore, a solution seems necessary to prevent exploitation and resolve other ethical concerns while ensuring sufficient supplies of human eggs for research. A brief review of legislation in different countries shows the existing diversity and controversy over compensating human egg donation for research purposes. While in more economically developed countries procreative liberty and consumer orientation seem to be defensible, in some developing countries, where concerns about exploitation exist, adopting a more regulated approach to assisted reproduction is more prudent and wise. Egg sharing is a program that has been proposed to solve both the ethical problems of purchasing eggs and the shortage of human egg supply for research. In developing countries, however, regardless of whether the egg sharing or the monetary compensation model is adopted, some steps should be taken to guarantee the ethical nature of this practice. These steps include ensuring the existence of independent institutional review boards (IRBs), confirming the validity of all steps in the process of obtaining informed consent, and ensuring the existence and viability of independent supervising and auditing bodies.

**Keywords:** *egg donation, research ethics, purchasing human eggs, compensated egg donation*

## Introduction

Monetary compensation for human body parts used in treatment or research remains fiercely debated throughout the world. The commercialization of obtaining several body parts raises serious concerns, for instance kidneys for transplantation, blood for transfusion, or even human embryos or fetuses for treating infertility or for use in research. Similarly, paying women who donate eggs for research is among the most controversial issues of modern medicine (1-6).

When it comes to egg donation, in addition to the previously mentioned concerns about commercialization of human body parts, other issues about women's health and rights must also be taken into consideration. Potential exploitation of women as research subjects has frequently raised major ethical and legal concerns. Egg donation is a classic example of such a potential (7).

The wide array of different and contradicting guidelines, regulations and opinions, which originate from different cultural, religious and theoretical backgrounds, has created a maelstrom around the issue of egg compensation.

During the past decades, almost all the contributors to this debate throughout the world have tried to suggest global solutions for the aforementioned ethical and legal concerns; it seems, however, that different cultural and socio-economic contexts and backgrounds necessitate different approaches to the same issue. This article argues that in more developed and prosperous countries highlighting procreative liberty seems to be defensible, but in some developing countries, where concerns about exploitation exist, adopting a more regulated approach to assisted reproduction is more prudent and wise.

### *Where the eggs are needed*

In general, donated human eggs are used for assisted reproduction, but there are also various types of research in which eggs are needed. The most prominent types of such research are embryonic stem cell (ESC) research and somatic cell nuclear transfer (SCNT).

Embryonic stem cell research (ESC) research has mostly occurred using surplus embryos remaining from infertility treatment (8), whereas obtaining ESCs with sufficient genetic diversity to study a broad range of diseases will require that new lines be created. Moreover, in order to avoid immune reactions in future therapeutic applications, researchers will need embryos that are produced by SCNT (4). Other types of research that use human eggs are physiological studies and studies on early human development.

### *Medical risks of egg donation*

After a workshop held in 2006 by the Institute of Medicine and the National Research Council of

the National Academy of Sciences (NAS), the Committee on Assessing the Medical Risks of Human Oocyte Donation for Stem Cell Research published a report according to which the medical risks of human egg donation can be divided into three groups (9):

*The risks of ovarian hyperstimulation:* The process of egg donation begins with the egg donor taking doses of hormones aimed to increase the number of eggs that can be retrieved. This ovarian stimulation may cause a number of health problems, the most important of which is ovarian hyperstimulation syndrome (OHSS), a condition characterized by signs and symptoms such as abdominal discomfort and mood swings in the mild form; increased ovarian size, ascite (accumulation of fluid in the abdominal cavity), abdominal distension and pain, nausea, vomiting, and diarrhea in the moderate form; and more severe signs and symptoms such as accumulation of protein-rich exudates in the peritoneum and pericardial spaces, breathing difficulties, increased concentration of red blood cells, kidney and liver problems, and, in the most severe cases, formation of blood clots or kidney failure, and finally death (10). About 0.1 to 0.2 percent of women taking ovarian stimulation drugs experience severe OHSS and a smaller percent of them experience life-threatening complications. For example, about 1.4 out of every 100,000 women undergoing an in vitro fertilization (IVF) cycle experience kidney failure. In addition, since a large percentage of the serious complications of OHSS seen in IVF patients are related to hormonal changes caused by pregnancy, it is predictable that the OHSS risks are lower for egg donors than for women involved in IVF. There is also concern that the use of ovarian stimulation drugs may lead to an increased risk of hormone-dependent cancers, particularly, breast, ovarian, and uterine cancers. The data to date do not support a significant relationship between such drugs and an increased prevalence of these cancers, although the possibility has not yet been excluded. Concern has also been raised about the potential effects of ovarian stimulation on the donors' long-term fertility, but at present there is no evidence that this is true.

*The risks of egg retrieval surgery:* Complications associated with anesthesia, or other surgical complications like infection and ovarian torsion, are extremely rare and even more so among egg donors compared to women undergoing IVF.

*The psychological risks of egg donation:* The potential psychological problems include the side effects of ovarian stimulation drugs, which fade away after the procedure is complete, and the psychological (and even spiritual) issues related to

the nature of this procedure. Moreover, there are concerns about the long-term effects of egg donation on the donor's well-being and fertility.

The committee mentioned that the health outcomes of egg donation are still unclear and there is a need to continue to gather information on the donors after the procedure and to observe them for potential long-term results (9). Some unproven concerns about long-term adverse effects of egg donation have been raised by other authors. Among these, cases of colon cancer in young women who had previously donated their eggs are noteworthy (11, 12).

The above-mentioned evidence and facts show that there are some rare but undeniable health complications that can be attributed to egg donation. Also, it should be noted that imposing burdens on egg procurement for research should be considered with more prudence compared with (infertility) treatment. There has been some criticism concerning the clarity of informed consent obtained in these cases, (13) but if proper informed consent has been given, research egg donation and egg harvesting cannot be considered unethical on account of the possible complications.

In summary, one can conclude that egg donation is a reasonably safe procedure, and the potential adverse medical consequences do not validate its exclusion from the list of acceptable research interventions, given that it is likely to yield important benefits to others.

#### ***The term purchase versus compensation***

Theoretically speaking, there are ethical differences between "purchasing human eggs" and "compensating egg donation". In practice, however, there seems to be major overlaps. Regardless of what the procedure is called, in this article we examine a regulated system of payment to egg donors, or providing them with other services such as free or reduced rate infertility treatment, which leads them to agree to egg donation they otherwise would not accept. It would seem that this compensation is significantly more than the direct costs imposed on the donor, as is the case in other research settings. It should be mentioned that this is true only in developed countries and when surplus eggs remaining from infertility treatment are involved.

Given the unacceptability of trading human body parts, and the regulated nature of the payments we consider as ethical, we prefer to use the term compensation rather than purchase when discussing the procedure with potential donors or in public media.

The term "purchase" has been used in some parts of this article in order to clarify the exact meaning and differentiate it from reimbursement of direct costs. Conversely, no significant distinction has been drawn between the terms "donor" and "provider" as suggested by Baylis and McLeod (2).

#### ***Arguments against purchasing human eggs for research***

The main arguments that have been put forth by opponents of purchasing human eggs are as follows:

*Commodification of the human body:* One of the main objections against purchasing human eggs is that this practice leads to the commodification of human body parts, which is a violation of the very principle of human dignity (14). This is a real concern in an unregulated setting where the price is determined by brokers and poor women are coerced to donate their eggs. Moreover, payment should not be so high as to turn donation into a source of income or give it a commercial nature. Egg donation should still preserve its altruistic and honorable spirit, which seems to be possible if the stepwise approach (see below) is adopted.

*Undue inducement:* Another major concern in economically disadvantaged societies is undue inducement, and the absence of research ethics institutions and regulatory and observatory bodies in such communities can lead to human tragedies (15). However, in well-regulated settings, with providers who are protected by law and ethical institutions and know their rights, a "limited and regulated" payment will not lead to undue inducement. It has also been argued by Klitzman (1) that imposing constraints on egg donation out of concerns about undue influence may indicate a degree of paternalism (1).

*Exploitation:* Considering the aforementioned medical and psychological risks and burdens imposed on egg donors, it has been argued that purchasing human eggs for either treatment or research can lead to exploitation of underprivileged women. As a matter of fact, reported experiences of poor women in some countries, especially developing ones, support this argument. In some cases, frequent donations with the intention of earning more money leads to major health problems. In addition, the money does not usually go to the donor, but to the husband or another dominant member of the family who takes advantage, sometimes to solve the financial problems of the whole family. It should be noted, however, that this form of exploitation cannot be attributed entirely to the monetary compensation of egg donation. The absence or inadequacy of safeguards such as informed and voluntary consent, supportive rules, regulations and regulatory bodies lead to various forms of exploitation. Therefore, existence of these safeguards can minimize exploitation of vulnerable women, although it should be mentioned that the root causes of exploitation in such societies are poverty and power imbalance in families.

#### ***Arguments in support of purchasing human eggs for research***

As a rule, participation in research is compensated; for example, it is customary for healthy

subjects in phase 1 clinical trials to get paid. In many cases, the compensation is enough to attract people to an unlikely competitive market of being a human research subject. Rationales for such compensation include boosting recruitment by offering an incentive to participate in the research, minimizing financial sacrifice on the part of subjects, eliminating feelings of inertia and distrust, and reimbursing subjects for their time and inconvenience (16).

It is acceptable and perfectly legal to compensate healthy human subjects (even children and other susceptible individuals, with added safeguards naturally) for participation in medical research. Consequently, some argue that there is no reason to exclude a certain kind of participation from the established reimbursement norm (1, 17). In cases of modest compensation, which usually is the case in research settings, no undue inducement takes place because a fairly small amount of money is unlikely to remove the potential donors' free will (17).

In the clinical setting, egg donors are usually paid. Therefore, it seems rather unfair if research subjects receive a smaller sum compared to others undergoing the same procedure in private clinical practice (1). Crocchin (17) further argues that if compensation for egg donation in research settings is regarded as coercion, the autonomy and free will of all egg donors and healthy human research subjects will be in doubt (17).

As a matter of fact, a major limitation to research is women's reluctance to donate their eggs without compensation. It has been reported that even after costly advertisement, prestigious academic centers, have not succeeded in convincing women to donate their eggs altruistically, but centers that paid donors were able to recruit a sufficient number of donors (1, 5). Lack of donors causes delays in the progress of certain research aimed to find vital cures. This delay possibly deprives many patients from treatments they need, which raises some concerns about social justice. Therefore, as the proponents of compensated egg donation claim, it serves the common good to allow such payments (1).

#### ***Rules, regulations and guidelines***

To demonstrate the diversity of opinion on this topic throughout the world, a brief overview of the related rules, regulations and guidelines in three countries with different cultural backgrounds and legal systems is presented here: United States of America, United Kingdom, and Iran. It should be mentioned that all these countries boast noteworthy research programs and achievements, as well as ethical and legal controversies on the very issues of hESC and SCNT

In the USA, professional and legal positions towards egg donation compensation are divided. On one hand, there are strong objections, for

instance in 2004, California's stem cell law prohibited payment for research egg donors (17). Subsequently, in Massachusetts, new legislation was ratified in 2005 which forbids monetary compensation or "valuable consideration" in the case of research donors and requires that any woman undergoing egg retrieval should receive the following documents: 1) an all-inclusive "informational pamphlet" on the potential health risks associated with the egg retrieval process, and 2) an obligatory "informed consent form" (17). In the same year, the National Academy of Sciences (NAS) Guidelines for Human Embryonic Stem Cell Research took the position that no payments should be provided to egg donors other than reimbursement of direct expenses. In 2007-2008, however, the NAS changed its stance in this regard to some extent, permitting some out-of-pocket reimbursement to egg donors (1, 17, 18). In 2008, Michigan law concerning hESC research only permitted use of surplus IVF embryos in cases of approved research (17). Similarly, in 2009, the National Institutes of Health (NIH) Guidelines on Human Stem Cell Research stated that the IVF embryos created for research purposes are not eligible for NIH funding (18).

On the other hand, in 2009, New York approved compensation for research donors in that state (19). The American Society for Reproductive Medicine (ASRM) also supports compensation for research donors (20); nonetheless, in an attempt to avoid "undue inducement," payments of more than \$10,000 are considered inappropriate.

In the United Kingdom, the Human Fertilization and Embryology Authority (HFEA) does not allow payment to egg donors, unless they participate in the so-called 'egg-sharing' program, which means that women undergoing IVF treatment donate their spare eggs to be used for reproduction or research purposes and are compensated by free or reduced rate treatment (21, 22).

In Iran, according to the National Ethical Guidelines for Biomedical Research, only surplus embryos remaining from infertility treatment should be used in research, and it is forbidden to produce human embryos solely for research purposes (23, 24). The existence of this guideline does not eliminate all the concerns about this practice in Iran. According to the author's experience and conversations with physicians and lawyers working in major infertility clinics in Tehran, these guidelines are not recognized and observed as solid national policies and mandates. Instead, such clinics prefer to operate under legal advice of their consultants which are based on two main sources: first, the formal legislations, which appear to be insufficient and incomplete, and second, the religious decrees issued by religious authorities that help practitioners to solve their ethical and legal problems. There are, however,

some ethical issues and concerns in different aspects of clinical practice in such institutions.

As a matter of fact, the current system of recruiting donors and retrieving eggs for infertility treatments may raise some concerns about the possibility of emerging egg donors undergoing repetitive and frequent periods of egg retrieval. Under the circumstances, the validity of the informed consent for both treatment and research purposes also needs improvement. Furthermore, researchers' knowledge and their attitude toward the above-mentioned guidelines have not been assessed and are subject to reasonable doubt. It seems that in Iran, as in some other developing countries, the main ethical issues regarding human egg donation, both for infertility treatment and for research, are the insufficiencies in the process of obtaining informed consent and ethical and legal supervisions and audits. It should be added that although research ethics committees have been established in almost all major research institutes in Iran, their independency and efficacy are not always verifiable.

This brief review of the legislations in different countries demonstrates the existing diversity and controversy over purchase (or compensation) of human eggs for research purposes. It also shows that concerns of possible exploitation and undue inducement are more serious and noteworthy in developing countries than in more economically developed countries.

#### ***Suggested solutions***

***Egg sharing:*** As described above, egg sharing is a program that has been proposed to solve both the ethical problems of purchasing eggs and the shortage of human egg supply for research. Critics have pointed out that in egg sharing, the ability to obtain informed consent is jeopardized because women who seek infertility treatment are sometimes in a desperate mindset to have a child; therefore, they might accept such donations without fully considering all the implications and consequences (25).

Although the egg sharing system seems to provide an ethically approved model for obtaining human eggs, precautionary measures should be taken to prevent exploitation and coercion, especially in developing countries.

***A stepwise approach:*** As mentioned above, the proponents of purchasing human eggs (or compensating egg donation) argue that a modest compensation would not influence the potential donors' free will. Nevertheless, this is not true in low- or even many middle-income societies, considering the urge of poverty and lack of gender equality, which may result in a coercive effect on females in the family to obtain money by selling their eggs.

Additionally, the egg sharing model cannot eliminate exploitation and coercion in such communities. Hence, compensation or egg sharing seem to be justified and ethically acceptable only after all of the following steps are taken:

1. Ensuring the existence of independent institutional review boards (IRBs) that follow international standards in evaluating all research proposals, their scientific design and the associated risk-benefit ratio from the ethical standpoint.
2. Confirming the validity of all the steps in the process of obtaining informed consent, including disclosure (by supplying comprehensive and well-designed pamphlets), understanding (especially of illiterate donors and ethnic minorities), and voluntariness (through appointing a trained and independent committee to assess each case).
3. Establishing clarified and defined legal and regulatory limits on all sensitive aspects of the process, including restrictions on payment and the frequency of donation for each donor.
4. Ensuring the existence and viability of independent supervising and auditing bodies.

***Restrictions on compensation:*** Payment should not be so high as to turn egg donation into a source of income or give it a commercial nature, and the act should preserve its altruistic and honorable spirit.

In the United States, the payment proposed to research egg donors is a fraction of the amount offered to reproductive egg donors (\$1000-1500 for research versus \$5000-10000 for reproduction) (16, 19). This amount cannot be the same in different countries, given the differences in income and cost of living. Accordingly, it seems to be reasonable that an independent committee determines the limits of such payments in each country.

#### ***Disclaimer***

The opinions expressed here are the author's and do not reflect the policies and positions of the National Institutes of Health, the U.S. Public Health Service, or the U.S. Department of Health and Human Services.

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