Human Oocyte Research
The Ethics of Donation and Donor Protection

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Questions of ethical research conduct have particular relevance for investigation using human reproductive materials. In recent years, few undertakings have generated as much controversy as donating oocytes for research. Placing this research in the context of ethical principles offers assistance in resolving ethical concerns regarding this work.

The Belmont Report provided an ethical framework for “human subjects” investigation, thereby delineating bounds between clinical practice and research. Expanding on these principles, several requisites for ethical clinical research conduct have been proposed that include assessing the investigation’s value, providing informed consent, establishing a favorable risk-benefit ratio, and ensuring fair participant selection. Ethical research conduct necessitates adherence to these principles, and research involving donated oocytes significantly challenges this effort, particularly as it relates to protecting donors from detrimental physical and psychological effects and to providing fair and equitable compensation to donors for their research participation.

Social Value and Scientific Validity (Nonexploitation)
Clinical research should be performed only if it improves the well-being of society, increases the global knowledge of disease, or both. Investigations involving human oocytes, including the development of stem cell lines, remain a worthwhile endeavor with tremendous potential to provide novel treatments for debilitating diseases. Accordingly, human oocyte research can be justified by a social and scientific priority to advance knowledge about oocyte biology and to generate potential therapies. However, the implications of this work must be conveyed carefully so as not to exploit prospective donors by misrepresenting the perceived benefits for humans.

Informed Consent (Respect for Autonomy)
The Belmont Report proposes 2 basic tenets to protect human participants: to treat individuals as autonomous agents and to protect those participants with diminished autonomy. This requires that research participants consent voluntarily after being provided sufficient information about the purpose, the process, and the potential risks of research participation. Additionally, informed consent requires that participants comprehend the information provided, a function of maturity and intelligence. For centuries, the law has asserted that individuals lacked informed decision making capacity prior to age 7 years, whereas those older than 14 years were able to make life choices. More recently, the age threshold for consent has been intensely debated. Current federal law governing research requires that legal adult status be attained (typically ≥18 years) to consent to study participation. It remains unknown whether the decisions of younger adult women (18 to 20 years) considering oocyte donation for research would be qualitatively different from those of older adult women (≥21 years). Consequently, the selection of research participants should ideally follow guidelines established for clinical oocyte donation thereby preferentially selecting donors between the ages of 21 and 34 years. Minors (<18 years) should be excluded from donating oocytes for research purposes.

Informed consent further requires the women donating oocytes for research participate voluntarily and without coercion or undue influence. Coercion involves an overt threat presented to obtain compliance. Although coercion may occur as a means to obtain human oocytes for research, a more likely scenario involves undue influence, particularly the potential for undue financial influence. To reduce this potential, the National Academy of Science and the California Institute for Regenerative Medicine guidelines prohibit compensation for oocyte donation. Appealing to altruism, this prohibition may reduce undue influence at the expense of violating justice and fairness to study participants.

Potential oocyte donors should be aware that research participation is not a condition for receiving medical services. Furthermore, it remains imperative to ethical research conduct that fee scales are not contingent on research participation. Oocyte sharing, e.g., offering a woman undergoing assisted reproductive technology a reduction in fees if she donates a portion of her oocytes to research, has been pro...
posed as a means to recruit donors. In this context, clinical care and research become indistinguishable, for medical services and fee schedules are directly related to research participation. Thus, the ability to obtain informed consent is diminished because undue influence cannot be eliminated. Women participating in oocyte sharing arrangements have reported that the desire for a child led some to donate oocytes for reproductive purposes without fully considering the potential risks and burdens. However, the pervasiveness of this emotion remains unknown. Moreover, it remains essential to inform potential donors of the experimental nature of oocyte research when a candidate considers study participation. In particular, if a woman elects to donate oocytes for the possible development of a stem cell line, the investigator must explicitly counsel the woman that stem cells have undetermined utility and must not overestimate the potential benefit that the contribution may have on humanity.

**Favorable Risk-Benefit Ratio (Nonexploitation, Nonmaleficence, and Beneficence)**

Oocyte donation involves complicated treatments, significant time to coordinate menstrual cycles, numerous office visits, painful injections, and ultimately anesthetic and surgical risks at the time of oocyte retrieval. To date, there is no conclusive evidence linking fertility drugs to breast, endometrial, or ovarian cancer risks. However, the risk of severe ovarian hyperstimulation syndrome is not insignificant (approximately 0.5%-5%) and is associated with considerable morbidity including abdominal ascites, acute renal failure, hypercoagulability, thromboembolism, and pleural effusions. Furthermore, oocyte retrieval may result in ovarian adhesion formation, thus reducing future fertility.

In addition to physical risks, psychological burdens associated with donating gametes should not be overlooked. Unlike other tissues, oocytes hold remarkable significance, corresponding, in the view of some, to the sanctity of human life. As a result, it is not surprising that the donation of oocytes to research may have a long-lasting psychological effect on donors. Clinical oocyte donors frequently report negative feelings from not knowing the pregnancy outcome of their donation. Women who donate oocytes for research may experience similar distress. Consequently, donors must be protected (nonmaleficence) from lasting psychological harm that their oocyte donation for research may cause. Current clinical guidelines maintain that donors and their partners, if applicable, should undergo psychological evaluation including structured interviews by qualified mental health professionals. Because current evidence is lacking to adequately address the psychological implications of this process, particularly among younger donors (18-20 years), formalized study with several years of follow-up should be incorporated into research protocols to assess for lasting psychological effects.

For women who are undergoing assisted reproductive technology, oocyte sharing (donation) presents the risk of reduced assisted reproductive technology–cycle success, by decreasing the number of oocytes available for fertilization. In the end, investigations may not benefit from this arrangement either because there would be a moral obligation to use the highest quality oocytes for clinical care, while preserving poorer-quality oocytes for research purposes. Immature oocytes or oocytes failing to fertilize following assisted reproductive technology could be used for scientific investigation, thus reserving high quality oocytes for clinical use. However, these oocytes are often abnormal and rarely develop healthy stem cells for research.

**Fair Participant Selection (Justice)**

Determining who benefits from research and who bears its burdens is central to establishing justice in research. Many contend that the widespread use of oocyte donation for reproductive purposes in the United States has been largely due to the legal and social acceptability of compensating women for oocyte donation. This perception has been supported by the availability of few anonymous donors in countries where compensation has been outlawed. However, oocyte donors continue to report that their primary motivating factor is an altruistic desire to help others and not financial compensation.

Traditionally, 2 types of financial incentives have been available to oocyte donors for clinical use: direct monetary compensation and oocyte sharing. In clinical practice, isolated accounts of agencies offering $50 000 for oocytes from women with specified physical, ethnic, and intellectual characteristics have been reported. This excessive compensation leads to undue inducement and exploits women, for some may agree to provide oocytes in response to financial needs, disregarding procedural risks. Furthermore, potential donors may censor critical health information to increase the likelihood of being selected as a donor, thus compromising clinical care and thwarting research endeavors.

Despite dramatic departures from typical payments, in 2006 the average clinical oocyte donor received less than $5000 in compensation for the time, inconvenience, and discomfort associated with the process. Monetary compensation for any oocyte donation has been criticized for making human gametes a commodity and thus devaluing human life. However, reasonable financial compensation is grounded in fairness to donors in exchange for the burden borne on behalf of the recipient or society in the case of donation for research. Monetary compensation in proportion to the time and the burdens associated with the process should not vary according to the planned usage of the oocytes. Nevertheless, the National Academy of Science and the California Institute for Regenerative Medicine guidelines maintain that women who donate oocytes for research purposes should not receive payments to avoid financial conflicts of interests and consequently undue influence.
sition violates the principle of fairness to donors for 2 reasons: oocyte donors encounter physical and potential emotional risks and participants in other research endeavors routinely receive compensation commensurate with their time and effort in these trials. Why should women donating their oocytes for research be any different?

Conclusions

Oocyte donation for research purposes will continue to come under increasing scrutiny as the science progresses. Understandably, many argue that oocyte research cannot be justified because it involves greater potential risks to donors than the potential benefits that may be attained at the present time. This is most recognizable when considering younger oocyte donors (18 to 20 years). However, oocyte research is ethically justified by established ethical principles. The equipoise of human oocyte research rests on advancing biological knowledge and generating potential therapeutic applications, while protecting prospective oocyte donors. This occurs by obtaining informed consent free of undue influence and coercion from those capable of giving this consent; by providing psychological counseling and long-term support to reduce untoward emotional effects; by separating research endeavors from clinical care; and by providing reasonable financial compensation for the time, pain, and risks associated with participation. Research involving donated oocytes including somatic cell nuclear transfer represents the leading edge of reproductive research. It is therefore not surprising that oocyte donation for these purposes evokes emotion and controversy. Nevertheless, oocyte research conducted in accordance with established ethical principles provides justification for furthering these endeavors and for the protection of potential oocyte donors.

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REFERENCES


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