Donating spare embryos for stem cell research

Ethics Committee of the American Society for Reproductive Medicine

Embryonic stem cell research is an ethically acceptable use of human embryos that are in excess of those needed to meet the fertility goals of patients. The ethical basis for this view and issues to be considered during the informed consent process for the donation of spare embryos are developed in this document. This 2008 report replaces the Committee's 2002 report, Donating Spare Embryos for Stem-Cell Research. Birmingham, Alabama

1. Embryonic stem (ES) cell research is an ethically acceptable disposition for human embryos in excess of those needed to meet the fertility needs of patients.
2. The final decisions on the donation of embryos to ES cell or other research must occur after the patients' infertility needs are met or the patients discontinue therapy.
3. The consent process should inform donors of the nature of ES cell derivation; the specific research project, if known; source of funding; potential commercial value; and anticipated clinical applications. Policies on confidentiality and maintenance of the donors' privacy should be in place and presented as part of the consent process.
4. Whenever possible, someone other than the treating physician should pursue requests for embryos for research purposes. Patients should be informed that refusal to participate will not affect medical care and that embryos used for research will not be transfered to a woman's uterus for possible pregnancy. They should be informed of financial incentives, if any, that the physician has in the research.
5. Embryos should not be bought or sold with a monetary exchange.

The ability to isolate and culture human embryonic stem (ES) cells, which was first reported in 1998, has opened a promising area of medical research (1). Derived from the inner cell mass of blastocyst-stage embryos, pluripotent ES cells give rise to all cell types in the human body and are thought to be able to proliferate indefinitely in an undifferentiated state (2). Researchers predict that, if coaxed to differentiate in culture, ES cells can be used to create specialized cells to treat a wide range of diseases and conditions, including Parkinson disease, Alzheimer disease, cancer, spinal cord injury, and juvenile-onset diabetes. Other envisioned uses of ES cells include research to understand cell specialization and the development and testing of new drugs (3).

Human ES cell research has provoked considerable discussion about ethics and policy. Among other commissions, the National Bioethics Advisory Commission considered the question of federal funding of ES cell research in 1999 and recommended that the government fund both the derivation and use of ES cells from spare donated embryos. The Clinton administration proposed funding only the use of ES cells, and the National Institutes of Health subsequently issued guidelines to oversee the process. Before any grants were made, however, a change of administration occurred. After further review of the issue, President George W. Bush announced on August 9, 2001, that the administration would consider for funding only those proposals using human ES cells from cell lines that had been derived and cultured by that date (4).

Although this decision opened the door to fundable research, many scientists have questioned whether the preexisting cell lines would be adequate for the research or therapies to which they might lead. Privately funded investigators are likely to seek additional donated embryos to obtain new ES cell lines for research in their own laboratories. New sources of embryos will enable investigators to study the derivation process itself, secure more cells from the initial embryo source if necessary, and culture cell lines from varied genetic sources. In addition, the human ES cells derived before August 9, 2001, were cultured in their undifferentiated state on a feeder layer of embryonic mouse cells, which renders these cell lines unacceptable for clinical trials. Presumably new cell lines will be needed for clinical trials to commence.

A primary source of embryos for future ES cell research is likely to be embryos donated by couples undergoing IVF who no longer want or need their embryos for fertility treatment. We consider here the conditions under which spare embryos ethically may be made available to researchers seeking ES cells. This consideration is preceded by a summary of differing perspectives about the ethics of embryo research.

ETHICS OF HUMAN EMBRYO RESEARCH

Human embryo research has elicited diverse and conflicting perspectives since the early days of in vitro fertilization. Discussions about the human embryo are frequently framed in terms of the embryo's moral status. An important distinction arises between those who regard the embryo as a person with all the protections accorded to fellow members of the human community and those who regard the embryo as deserving respect as a potential human being but not the same respect accorded to persons.

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Those who believe the embryo has the moral status of persons expect that the embryo should be accorded all the rights of these individuals. The embryo is vulnerable, under this perspective, and needs protection. Some believe that this status begins during fertilization, when the DNA from the female and male gametes combine to create an entity with a novel genetic composition. Others believe that the status begins later, when the primitive streak begins to develop approximately 14 days after fertilization and when the embryo will, if it survives, develop into a single individual.

Most of those who believe that the embryo has a status distinct from adults and children regard the embryo as a potential human being worthy of special respect but not entitled to the same rights as persons. This perspective is applied particularly to the embryo used in research, which ranges in development from a single cell to hundreds of cells, has no nervous system, and has a limited chance of developing to birth. The possibility of twinning or regression to a nonviable entity up to the fourteenth day after fertilization is consistent with the notion that the embryo lacks individuality. Moreover, according to this point of view, the early embryo lacks the criteria traditionally equated with human status.

The Ethics Committee of the American Society for Reproductive Medicine (ASRM) has consistently held to the second perspective, which regards the embryo as a potential human being worthy of special respect (5–8). The ASRM Ethics Committee regards embryo research as ethically acceptable if it is likely to provide significant new knowledge that will benefit human health and if it is conducted in ways that accord the embryo respect. The Ethics Committee, along with commissions and advisory bodies from around the world, have developed core expectations about how research using embryos may ethically be conducted (8, 9). Among other things, it is expected that patients must give informed consent to donate their spare embryos for research, embryos should not be kept cleaving more than 14 days after fertilization, and there should be no buying and selling of embryos. It is also expected that the investigator bears the burden of justifying the worthiness of the research, uses the smallest possible number of embryos, submits proposals to review by an Institutional Review Board, has no satisfactory alternative to using embryos, and expects important clinical data to accrue from the research.

The ability of scientists to isolate and culture human ES cells has evoked renewed discussions about the ethics of embryo research. Advocates of ES cell research argue that preimplantation embryos would be discarded and that it is appropriate to gain some benefit from them. In light of the potentially significant impact on regenerative medicine, they argue that it may even be morally obligatory to pursue this research. They also note that donation for embryo research is an extension of the patients' authority over the disposition of embryos.

Critics, on the other hand, argue that research causing the destruction of embryos is wrong. In addition, they argue that stem cells derived form sources other than embryos also hold potential for diagnostics and therapy. They also express concern that the research will lead to the treatment of embryos as commodities and of a consequent diminished respect for embryos. The matter of whether embryos may ethically be created for ES cell research through in vitro fertilization or somatic cell nuclear transfer remains a topic of continued debate and elusive consensus (10–15).

INFORMED CONSENT AND THE DONATION OF SPARE EMBRYOS FOR ES CELL RESEARCH

A distinct feature of ES cell investigations is the intent to derive cell lines that may continue to divide indefinitely and be used by researchers for many years to come. Cell lines eventually may have considerable commercial value. In addition, they may potentially be traced to donors (10). For these and other reasons, it is appropriate to revisit guidelines about what should be conveyed to patients in the donation process, when, and by whom. Evidence exists that donation for research is a preferred option for patients who have spare embryos (16). These guidelines aim to protect the autonomous interests of patients faced with deciding the disposition of embryos they no longer want or need.

What Information to Convey to Potential Donors

Informed consent is a basic requirement for the ethical conduct of all human subjects research, including studies using human embryos. Patients who donate embryos may take a range of considerations into account in making their decisions (17–19). During the consent process for embryo donation for research, patients should be told of the risks and benefits of donation. For example, a risk might arise if the patients were later to wish they still had the embryos available for their fertility efforts. A benefit might be the satisfaction of knowing that they have contributed to research designed to advance medical therapies. Patients should also be told of the purpose and nature of the research and whether the research is expected to have commercial value. They should be told that they may change their minds about donation at any time until the experiment begins, that their status in the infertility program will not be affected if they do not donate spare embryos, and that no embryos used in the study will be transfered for pregnancy (8).

In the case of donation for ES cell research, other considerations may also be relevant. Given the wide range of uses to which ES cells may be put, patients should be informed of the specific research project, if known, or at least of the category of anticipated research, such as reproductive research, development of therapies for disease, or product development. Patients should also know that ES cell research typically involves deriving cells from the inner cell mass of an embryo at the blastocyst stage, which leads to the embryo's destruction.

Potential donors also should be informed that the cell lines might exist indefinitely. They should be told that stem cells from embryos may have commercial value for a wide range

of research and clinical purposes and that they as donors will not share in the commercial value. The clinic should develop a policy on privacy and confidentiality of donations and present this as part of the consent process. If identifiers are attached to the cell lines, the donors must be informed of this and of steps taken to assure their anonymity. The male and female partners must agree on the disposition of their spare embryos. If they cannot jointly agree to donate embryos for research, the embryos should not be used for research.

When Consent Should Be Obtained

It is important that patients decide to donate embryos for research only after they have decided not to continue storing their embryos. Making separate decisions about no longer using embryos and donating them for research guards against pressure being placed on patients to donate embryos. When embryos are created, patients often stipulate what should be done with their frozen embryos in the event of future contingencies such as death, divorce, or no contact with the clinic. These directives usually involve donating the embryos to other patients, donating them for research, or discarding them. If no death or divorce occurs, the patients make a separate decision about what should be done with the unused embryos when their fertility needs are met or they end their reproductive efforts with those embryos. At this point the investigator has the opportunity to discuss more thoroughly the option of donating embryos for research.

Using only frozen embryos for research ensures that time passes between the creation of embryos for conception and their donation for research. Still, it is reasonable to expect questions eventually to arise about the donation of fresh spare embryos (20). Donation of fresh embryos raises the possibility that a physician might induce a patient to allow insemination of extra eggs so that they may be donated for research. Moreover, this increases the chance that decisions will be made quickly and later regretted by patients. Without evidence that fresh embryos are significantly preferable to frozen embryos for ES cell use, it is appropriate to use only spare embryos that have been frozen. In cases in which patients were opposed to embryo cryopreservation but not to embryo donation for stem cell research, it would be ethically acceptable to donate fresh spare embryos for such research. However, because the number of embryos created and frozen should be determined by the patients' clinical needs, it is incumbent upon the physician to confirm in such cases that the patients are fully informed about the clinical implications of their decision to donate fresh spare embryos.

In some situations, patients with stored embryos cannot be reached despite efforts to reach them. The Ethics Committee has previously concluded that programs may consider embryos to be abandoned if clinics have taken diligent steps to contact the couple, no written instructions exist, and more than 5 years has elapsed without contact with the couple (21). Abandoned embryos may be discarded, but they should not be used for research or donated to other patients without prior consent. In some cases, patients may have given consent to use spare embryos for research but were not informed of the possibility of ES cell research. The singular features of ES cell research make it advisable not to use such embryos for ES cell research unless patients have given specific advance consent for this use in case they cannot later be reached for a decision. Advance permission to use abandoned embryos for research may thus prevail for ES cell studies if the patients have been informed of the possibility of ES cell research.

Who Should Obtain Consent

Several advisory bodies have recommended that a person other than the fertility specialist should secure consent to donate embryos (2, 13). The rationale is that this will ensure that the patients' reproductive needs are foremost and avoid conflicts of interest when the fertility specialist is also the investigator. In some circumstances, however, this guideline may be difficult to follow. It is possible, for example, that the fertility specialist who knows the patients and is trusted by them may be better able to have a frank discussion with the couple about donation for research and may secure more informed consent.

Moreover, using a separate person to secure consent may be difficult if the physician is part of the research team. The possibility of undue influence by the physician will be lessened if the request for a donation is made after the patients decide to dispose of their embryos. Still, the fact that the physician is also a researcher is relevant information and should be conveyed to the patients along with a statement about incentives, if any, that the physician has in the research. The rule that the number of embryos created and frozen must be determined by the clinical needs of the patients and not by research goals is especially pertinent when the physician is both the fertility specialist and the investigator.

SUMMARY

The ASRM Ethics Committee affirms that it is ethically acceptable to derive and use ES cells in research to develop cell replacement therapies and to further other medical uses. This research should take place only within guidelines in place for embryo research in general and only under conditions that protect the free and informed consent of patients.

The members of the ASRM Ethics Committee have the following potential conflicts of interest:

Andrea Braverman, Ph.D., has nothing to disclose

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