

# AMERICAN ACADEMY OF PEDIATRICS

Committee on Pediatric Research and Committee on Bioethics

## Human Embryo Research

**ABSTRACT.** In 1996, a ban on the use of US Department of Health and Human Services funds for research on the creation of human embryos and research that involved the injury or destruction of human embryos was signed into law. This ban was partially reversed in 2000 when the National Institutes of Health announced it would fund selective research on human pluripotent stem cells. Given the potential benefits to society, research using human embryos is an issue that deserves additional consideration. The American Academy of Pediatrics believes that, under certain conditions, research using human embryos and pluripotent stem cells is of sufficient scientific importance that the National Institutes of Health should fund it and that federal oversight is morally preferable to the currently unregulated private sector approach.

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ABBREVIATIONS. DHHS, Department of Health and Human Services; NIH, National Institutes of Health; IRB, institutional review board.

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### INTRODUCTION

**H**uman embryos are defined as human organisms derived by fertilization from 1 or more gametes or diploid cells. Pluripotent stem cells are specialized subpopulation of cells capable of developing into most (ectoderm, mesoderm, and endoderm), but not all, human tissue and may be derived from human embryos. In 1996, a ban on the use of US Department of Health and Human Services (DHHS) funds for most research using human embryos was first signed into law and has been renewed annually. However, such research is still being conducted with private funds.<sup>1</sup> Opposition to the use of federal funds for research using human embryos is generally based on ethical concerns about embryo research, particularly related to the associated destruction of human embryos before or during research. Although it may not be possible to prevent all embryo research, the argument is that, at least, public funds should not promote this activity.

Research using human embryos, similar to research using human fetal tissue, has been and will remain a controversial issue. Reasonable persons in many segments of society have different opinions on this topic based on strongly held beliefs and value systems. Despite the possibility of important therapeutic advances resulting from research using human embryos or embryonic stem cells, some believe

that any activity that results in the destruction of human embryos is morally problematic. They argue that the ends do not justify the means. Opponents of research associated with the destruction of human embryos are not swayed by attempts to separate the research from the procurement of the necessary stem cells or from embryos discarded as part of the process of in vitro fertilization. This practice is morally questionable to them. Citing their personal and professional commitment to the well-being of embryos and fetuses, opponents of research using human embryos advocate for more emphasis on research using nonembryonic tissue.

One ethical concern related to research using human embryos involves how embryos may be acquired for research purposes and, thus, the moral complicity of researchers in such issues as discarding of embryos that are no longer needed from fertility clinics. The use of embryos that are no longer clinically needed may be less problematic than creating embryos explicitly for research. However, even the use of embryos that are no longer clinically needed can raise questions related to obtaining adequate informed consent from potential donors, ensuring the privacy of donors, decreasing potential or perceived conflicts of interest by those who may request the donation and concerns about undue financial inducement to acquire embryos.

Another ethical concern relates to the use of human embryos in research. Given the unique developmental relationship between embryos and human persons, the use of embryos may require special considerations to limit the research to important issues that cannot be addressed in other ways and to conduct the research within boundaries established to reflect appreciation for the special nature of human embryos. For example, the 1994 National Institutes of Health (NIH) Human Embryo Research Panel proposed a limit of 14 days after fertilization for the use of embryos for research. Although this limit may appear somewhat arbitrary, which the panel acknowledged, this limit was based on at least 2 important considerations. First, 14 days appears to be the limit after which twinning does not occur. Hence, before this date, it is more difficult to consider an embryo as a distinct, developing individual. Second, 14 days is a period before the development of the primitive streak, which eventually develops into the embryonic neural system. Although some have argued for limiting the use of human embryos in research to earlier or later stages of development, the NIH panel believed that this clearly defined number would address many of the ethical concerns

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The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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about the use of embryos while allowing research, albeit of limited scope. In effect, this choice reflects an argument that the early embryo before 14 days of development is not the equivalent of a fetus or person and, thus, may be used in research under certain additional conditions.

Despite the ban on federal funding, research using human embryos and pluripotent stem cells (cells that can give rise to a variety of tissue including but not limited to cardiac, neural, hematopoietic, and others) derived from human embryos or aborted fetuses continues to proceed exclusively through the use of private funds. The subsequent lack of regulatory oversight does little to address many of the ethical concerns, and the lack of federal funding may limit the potential for this research to be valuable to large segments of society, such as children. Proponents of lifting the ban on the use of federal funds for research using human embryos believe that such funding could facilitate greater scientific and ethical oversight. Federal funding would allow greater scrutiny of the value of this research through the peer review system. Any funding should also be contingent on strict adherence to guidelines about appropriate ethical limitations in the acquisition and use of embryos. Finally, federal funding could create incentives to direct research toward health issues that have important implications for children.

#### CONDUCT OF EMBRYO RESEARCH

As is the case for any type of research but especially research that involves living tissue or organisms, the questions being explored must be of compelling importance to justify the work. Advocates of the use of human embryos in research believe that there are research questions that justify the use of human embryos and that these questions range from those of tangible clinical value to those of more theoretical and long-term benefit. Potential research applications of importance to children include the following: 1) development of pluripotent stem cells and therapeutic use of specialized and differentiated cells; 2) creation of specialized cell lines for drug susceptibility, toxicity, and efficacy testing; and 3) research in normal and abnormal differentiation and development.

Recently, several investigators have successfully isolated and cultured pluripotent stem cells from frozen human embryos donated by couples who had previously undergone in vitro fertilization and whose additional embryos were no longer clinically needed.<sup>2</sup> Concrete benefits for children resulting from pluripotent stem cell research with human embryos are anticipated, including treatments for spinal cord and bone injuries, diabetes, primary or acquired immunodeficiencies, cancer, metabolic and genetic disorders, and a variety of birth defects. Research with human embryos that involves drug or toxin testing could benefit children suffering from toxicities of drug treatment and environmental pollutants as well as prenatal drug use disorders, such as fetal alcohol syndrome. Research using material derived from embryos also could be used in the study of

normal and abnormal differentiation and development, which could benefit children with birth defects, genetically derived malignancies, and certain genetic disorders.

An important long-term benefit of research using human embryos can be found in the field of teratology.<sup>3</sup> Experiments that involve exposing pregnant mice to a teratogen at specific times after mating and observing the resulting defects have demonstrated that early exposure can result in very specific developmental defects. Other research on mouse embryos has advanced the ability to evaluate gene function in the early embryo.<sup>4</sup> In the future, it may be possible to combine these approaches to obtain important insights into teratogenesis in humans. Specifically, there is the future prospect of studying the expression of specific genes in embryonic cell lines exposed in vitro to teratogens. Such research could potentially provide insights into the approximately 40% of anatomic defects in infants for which there are currently no explanations.<sup>5</sup>

#### ACQUISITION OF EMBRYOS FOR RESEARCH

Embryos are created as part of in vitro fertilization for couples for whom other means of bearing children have been unsuccessful. In brief, in vitro fertilization consists of obtaining oocytes (eggs) most often from the prospective mother (but sometimes from a donor) and fertilizing them under controlled conditions in the laboratory, using sperm obtained most often from the prospective father (but sometimes from a donor). Fertilized oocytes that appear viable are transferred to the uterus with the hope that 1 or more will implant and result in pregnancy. Because implantation is often not successful, a large number of embryos are usually created to allow for multiple attempts at fertilization and implantation. The generation of excess embryos is undertaken given the time, physical risk, expense, and emotional trauma associated with obtaining, fertilizing, and implanting oocytes.

The current practice of in vitro fertilization results in some embryos that are ultimately not needed clinically and, thus, discarded. These may include embryos that are abnormally fertilized, as evidenced by the presence of more than 2 pronuclei. Also, embryos suitable for implantation may be produced in excess of the number that can be returned to the uterus at one time. These embryos are usually frozen and, at the option of the donors, can be thawed later and transferred to the uterus. However, some individuals who go through the process of in vitro fertilization (potential donors) choose not to undergo additional embryo transfers and do not wish to have their embryos donated to other individuals. Such individuals or donors may be willing to donate their embryos for research.

#### OVERSIGHT OF EMBRYO RESEARCH

The American Academy of Pediatrics supports a policy that would permit donation for research funded by DHHS of frozen embryos produced during the process of in vitro fertilization that would

otherwise be discarded by the individual or couple (potential human embryo donors). The DHHS oversight process would allow research to be limited to questions of vital importance. The Academy also believes that all research on frozen human embryos should require institutional review board (IRB) approval and that informed consent should be obtained from all embryo donors. Study sections and IRBs should limit embryo research to the following conditions:

1. The embryos are already frozen and are no longer clinically needed.
2. There is a clear separation in the donor decision process between the decision by the donors to create embryos for infertility treatment and the decision to donate frozen embryos for research purposes after they are no longer clinically needed.
3. The decision to donate is strictly voluntary and without monetary inducements.
4. The physician responsible for fertility treatments is not to be the person performing the research on the same frozen embryos, and there should be no monetary relationship, ie, transfer of funds in the research project to the physician responsible for the fertility treatments.
5. There are to be no personal identifiers associated with the embryos used for research.
6. There are to be no restrictions placed by the donor on the type of research performed.
7. The research performed on these frozen embryos can be of no direct benefit to the original donors.
8. The embryo research does not involve research in reproductive cloning, transferring an altered embryo to a woman's uterus, or use of a human embryo in combination with other human or animal embryos.

A limit on the stage of development after which the use of human embryos is not allowed, such as that suggested by the NIH panel, is necessary. However, given the complexity of this issue, additional consideration of this limit is necessary.

The informed consent process for embryo donors should include the following statements:

1. All identifiers associated with the frozen embryos will be removed.
2. The donors will not receive any future information regarding subsequent testing or research on these embryos.
3. Cells or tissue developed from the embryos may be used at some future time for human transplantation research.
4. Cells or tissues derived from the embryos may be kept indefinitely.
5. The donated frozen embryos may be of commercial value, but the donors will not receive any financial or other benefits from any such commercial development.
6. The research performed on these frozen embryos is not intended to provide direct medical benefit to the donor.

7. The research will not involve the transfer of these embryos to a woman's uterus or involve reproductive cloning or combination of the embryo with any other embryo of human or animal origin.

Given the complex nature of the scientific and ethical issues related to research using human embryos, an additional oversight committee should be created by the DHHS to clarify scientific and ethical guidelines for such research and review proposed research to ensure compliance with these guidelines. Additionally, although current federal regulations for research address issues related to the donors, there are no clear regulations regarding the use of human embryos. Additional guidance for the use of embryos would be needed.

#### CONCLUSIONS AND RECOMMENDATIONS

Recent scientific advances, particularly those related to embryonic stem cells, have prompted the Academy and other groups to revisit the use of human embryos in research. Recently, the DHHS has suggested that the current law should permit the use of federal funding for research using human pluripotent stem cells originally derived from frozen human embryos. Similarly, the National Bioethics Advisory Commission has recently recommended that federal funding be made available for research on embryos donated with consent by couples who no longer need them for infertility treatments. The Academy believes that DHHS funding of selected research on human embryos would allow better mechanisms for peer review of the scientific objectives and review of ethical considerations. Finally, lifting the ban on this type of research would attract investigators to this area, which, along with the resources of the NIH, would accelerate the pace of research on health issues with important implications for children. This statement, however, does not take a position on research conducted with material from an aborted fetus.

The Academy recommends the following:

1. Congress and the president should reverse the current ban on DHHS funding of human embryo research and support the recommendation by the National Bioethics Advisory Commission to allow federal funding for research on embryos provided by consented donors after in vitro fertilization.
2. The DHHS should establish an oversight committee, in addition to NIH study sections and IRBs, to review compliance with scientific and ethical guidelines of all proposed and funded research on human embryos.
3. The DHHS should develop guidelines for IRBs about the appropriate conduct of research involving human embryos.

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