

The Ethics of Embryonic Stem Cells— Now and Forever, Cells Without End

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Surely every medicine is an innovation, and he that will not apply new remedies, must expect new evils.

Francis Bacon (1561-1626)

THE PROMISE AND POTENTIAL OF HUMAN EMBRYONIC STEM cell research evoke profound clinical enthusiasm¹⁻³; the embryonic human origins of such cells warrants an equally profound ethical concern. The ethical issues are not primarily matters of scientific fact nor of political belief. Consequently, these issues cannot adequately be addressed simply by reference to the biology of embryonic stem cells or the contemporary political context of stem cell research. To successfully make the case for developing the therapeutic potential of human embryonic stem cells, the biomedical community must engage these issues as genuine questions of morality and social policy. Just as an accurate understanding of stem cell biology is crucial to sound policy making, an accurate appraisal of the substantive and inseparable ethical issues is equally crucial. The biomedical community and society as a whole can answer these questions and justify the clinical promise of embryonic stem cell research but only by paying serious attention to the legitimate ethical issues.

Handcrafted or Secondhand?

The human fetus is derived from a fertilized ovum, essentially a single cell with the capability of producing every cell in the adult body. During development, human cells progressively differentiate. Simultaneously, the ability to form a wide variety of cells becomes progressively restricted. Embryonic germ cells give rise to gonadal tissue, forming ova and sperm in the adult.⁴ Almost by definition, these cells are pluripotent, in that they carry the genetic information for an entire human being. The thrust of current clinical interest, however, is not in the embryonic germ cell line that can give rise to future offspring (and whose potential modification or use raises independent ethical concerns⁵ that are not discussed here) but rather in the embryonic stem cells that give rise to the remainder of the adult organism. Embryonic stem cells are early, “universal” cells with the po-

tential to form virtually any somatic cell in the human body. Their clinical potential is equally universal.^{6,7} If research can overcome the remaining (and still substantial) technical hurdles, these cells would allow for the growth of transplantable organs in vitro.

Embryonic stem cells currently are collected from the primordial germ cells of embryos that have been aborted for unrelated reasons or from embryos that are left over from in vitro fertilization procedures and that otherwise would be destroyed.⁸⁻¹¹ Any tissue grown from these salvaged stem cells would, of course, normally face the same risks of rejection as any other genetically mismatched transplantation. However, by transferring the nucleus from a patient’s somatic cell into an enucleated human ovum, stimulating it to divide, and harvesting the resulting embryonic stem cells, new organs could be grown that would be a perfect genetic match.¹² Equally, cloned stem cells could be cultivated to replace portions of missing or diseased organs within the body, such as islet cells for patients with diabetes or myocardial cells for patients with cardiomyopathy. Even without cloning, embryonic stem cell lines could be antigenically altered and then grown without many of the standard antigenic tissue markers that currently prompt rejection. This would allow them to be not only universal within but also between patients. Such generically transplantable human cells and organs would no longer require immunosuppressive agents.

The distinction between “therapeutic cloning” (producing antigen-matched, cloned cells or organs for transplantation) and “reproductive cloning” (duplicating an entire human organism) is often emphasized in discussions of stem cell research.¹³ Yet whether the result is a cloned child or a line of cells, both procedures currently begin by creating a human embryo. To produce a reproductive clone of the nuclear donor, an embryo must implant and gestate in a womb. To produce therapeutically cloned stem cells for the nuclear donor, an embryo (blastocyst) must be dissolved and only the primordial stem cells retained and cultivated.

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See also p 3175.

The same is true of deriving a line of uncloned, antigenically null stem cells for therapy. These processes are hardly therapeutic for the embryonic clone. Like the term “therapeutic abortion,” the label sidesteps, but thereby underscores, a second fundamental ethical question: How shall ethicists, clinicians, and any individual concerned about these issues weigh the fate of the embryo, from which these cells are derived, against the therapeutic value to patients with real medical needs?

Ethically, does it matter that the therapeutic products of stem cell lines are derived from human embryos created solely for that purpose rather than salvaged from other doomed conceptions? Although there are arguments on both sides, one point is clear: Creating embryos for the sole purpose of obtaining stem cells cannot merit the moral warrants of “wresting value from tragedy” or “preserving human cellular life” that have been used to justify collecting stem cells from incidental abortions and unused embryos from *in vitro* fertilization procedures.¹⁴ There is a consensus that deriving embryonic stem cells from human embryos solely created to obtain embryonic stem cells faces a higher bar for justification than does the use of donated organs or cells.¹⁵ To clear this bar, proponents of therapeutic cloning must explain why it is morally permissible to initiate development of one human with the intent of truncating such development at an early stage for the benefit of another. Arguing that the natural high rate of loss of early embryos justifies further such truncation is invalid.¹⁶ While the natural loss of human embryos is not a moral tragedy, their intentional conception and diversion to meet another’s needs may well be.

Moral Status of the Human Embryo

The answer to these questions depends on the moral status given to the human embryo.¹⁷ This is a vexing question on which many religious and philosophical traditions take strong positions.¹⁸ Although human embryology is often brought to bear to defend particular positions, this is an issue about which biological opinion is neither decisive nor even necessarily pertinent. Biology may identify the species (eg, human) of an embryo, determine whether it is physiologically active (ie, alive), and define specific developmental milestones, each appropriate to the biological venue. However, the ethical implications of such biological facts—the moral status of early human embryos—remain firmly a matter for religious conviction and social values, tempered (hopefully) by clear philosophical thinking.

Fortunately, there has been a good deal of just such thinking over the last decades, both in biomedical ethics and by broadly based public policy commissions, which is worth applying to this topic. While there remain strong advocates at both extremes—for investing human embryos with all the moral rights and protections of persons “from the moment of conception”^{19,20} and for withholding full “personhood” status until well after birth²¹—an important development in this literature has been the emergence of one

view that has become widely endorsed as intellectually defensible: the “developmental view” of moral status.²²⁻²⁵ In this view, each individual acquires different moral interests, rights, and roles as he/she develops sentience, consciousness, and relationships justifying these protections. At every stage, by virtue of this developmental trajectory and the “symbolic” value of embryos as human beginnings, human embryos deserve “profound respect.”²⁶ What this means in the case of the use of embryonic stem cells for therapeutic means remains open to debate.²⁷ As the dominant position in US science policy settings today,²⁸ however, the developmental view is a position that advocates of embryonic stem cell use should be prepared to discuss, if only to respond to the ways in which it might be used against them.

One interpretation of such “profound respect” for the embryonic source of stem cells is respect for the “cellular dignity” of these embryos as symbolizing the personal autonomy society already honors in adults. This argument suggests that, just as slavery and disabling mutilation are paradigmatic affronts to human autonomy, intentionally conceiving and then hobbling the development of human embryos to serve another person’s needs should be counted as a breach of the “profound respect” they are due as symbolic persons. If it would be wrong for a woman to intentionally become pregnant and abort her fetus to harvest its stem cells for her own use, so too would it be symbolically disrespectful to intentionally conceive and then dissolve one’s embryonic twin to use its stem cells. Salvaging organs from the dead is one thing, arranging a death to obtain well-matched organs is another. From the perspective of the “profound respect” due human embryos, organogenic cloning is more analogous to the latter.

Ethical Costs of Omission

While the ethical issues of using embryonic stem cells need serious attention, equally a competent discussion cannot forget the costs of not using them. Consider the ethical difference between the following 2 scenarios: In the first, a child dies of pneumonia in 1900 because there are no effective antibiotics. In the second, potentially in the near future, a child dies of pneumonia, because antibiotics—although effective—are legally restricted. The medical outcomes are precisely the same and perfectly “natural,” but the ethical situations are drastically different. If any individual would intentionally restrict the development of a life-saving therapy, then he/she must be willing to shoulder responsibility for the consequent deaths. Similarly, if ethicists or the public would restrict the uses of embryonic stem cells, then they must then bear responsibility for those patients they have chosen not to try to save by this means.

Currently, patients die regularly because transplantable organs are unavailable.²⁹ There is no moral culpability in this: physicians are powerless. If stem cell research can provide the power to address this need, however, the claims of those patients become compelling. The dangers of eroding

the respect due human life must be balanced with the particular needs of real patients in jeopardy. A second major challenge for biomedicine and society is to decide how best to strike that balance. Ethical decisions are not limited by intent, rather they encompass all consequences, even those that many would strongly prefer to disavow. Accepting the “costs of omission,” the ethical balance becomes more faithful, though, alas, considerably heavier.

Collateral Effects

Either position on stem cell research also will have collateral effects. For instance, during the World War II bombing of a deuterium plant, an innocent Norwegian village was utterly (and unavoidably) destroyed. Yet, not destroying the plant might have had yet greater costs. Likewise, if embryonic stem cell therapy is prohibited, then living patients are implicitly devalued by striking the balance against their needs. In the process, this may unintentionally encourage black-market activity, resulting in riskier, unregulated therapies and an erosion of respect for the thinking behind the prohibition: exactly the erosion of values that the prohibition would be designed to protect. But if a medical therapy based on an unethical source is accepted, the door may be open to even worse problems. If physicians are allowed to create cloned embryos for organogenesis (and be paid for the service), would it be fair to prohibit women from getting paid to conceive and abort an early fetus for the same purpose? As complex and politicized as the dialogue might become, thinking out loud about these 2-edged implications must have to be part of any responsible public decision making about these issues.

Risks of Ethical Polarization

Ironically, it must be recognized that the ethical debate that is being advocated here can itself have collateral social risks. Nonembryonic stem cells are already in widespread and appropriate clinical use. Such use neither carries, nor deserves, any ethical stigma. Circulating hematopoietic stem cells,³⁰ for example, are routinely used to replace marrow-derived cells after chemotherapy for malignant cancers,^{31,32} particularly those of the breast.^{33,34} Such stem cells are derived from the adult patient and can be used in treating malignant cancers,³⁵ several autoimmune disorders³⁶⁻³⁸ (such as arthritis,³⁹ systemic lupus erythematosus, and scleroderma⁴⁰), corneal scarring,^{41,42} central nervous system diseases,⁴³⁻⁴⁵ and perhaps many other diseases.⁴⁶ These cells require neither dedifferentiation nor an embryo, and no ethical question is raised by their source, which is adult (usually autologous) cell donation.

If pluripotent stem cells—with a therapeutic potential equivalent to that of embryonic stem cells—could be derived from normal postpartum placental tissue or by “dedifferentiating” them from adult somatic cells,⁴⁷ then the current ethical debate should be moot. For instance, if a patient donates a single epithelial cell from the back of his/her hand

and that cell is then dedifferentiated and thereby creates a pluripotent stem cell without creating an embryo, then the symbolic value of human ontogenesis is no longer at risk.⁴⁸ However, if that scientific advance emerges in a climate already polarized by divisions over therapeutic cloning, it could face a generalized opposition to stem cell research that overlooks that crucial difference.

Currently, the scientific community remains ignorant of much of what regulates cell differentiation and dedifferentiation.⁴⁹⁻⁵² In restricted cases, however, dedifferentiation has already been accomplished in partially differentiated murine embryonic cells,⁵³ postnatal mouse⁵⁴ or rat⁵⁵ nervous system cells, and postnatal rat or human^{56,57} bone marrow cells. Similarly, postnatal human olfactory cells have been identified that are capable of remyelinating damaged, demyelinated rat spinal cord neurons.⁵⁸ The likelihood is increasing that pluripotent stem cells soon may be derivable from nonembryonic tissue. If patients are to welcome medical developments in tomorrow's clinics, then it is necessary to take utmost care to preserve moral space in today's discussions. Accordingly, clinicians, scientists, and ethicists must avoid premature polarization of these issues and clarify terms as they engage in ethical debates. Generic castigation of stem cell research, which may sensitize patients and jeopardize promising future therapy, is unnecessary and is ethically irresponsible. For the medical proponent, this means being more than a single-minded advocate for patient care; for the ethical critic, it means not stigmatizing all stem cell research with their otherwise valid concern.

Public Funding

All these ethical issues become heightened in the context of public funding for the research involved. By its nature, public funding raises its own independent ethical issue. Federal research funding compels the individual (from whom federal funding ultimately derives) to indirectly support public endeavors that the individual person may find ethically unacceptable. Federal agencies and legislatures have been sensitive to this issue, balancing it against countervailing public (and health advocacy group) support. As a result, the discussion is now set in the public context of a number of proposed regulations and legislative guidelines, both in the United States and globally.⁵⁹

In the United States, the past several years have produced 2 important administrative decisions regarding stem cell (or human embryo) research as well as the enactment of a federal law and numerous state laws. Excepting several state laws,⁶⁰ these all permit research using stem cells derived from salvaged human embryos. The possible use of embryos created through somatic cell nuclear cloning, however, is less clearly addressed in these policy proposals. With specific limitations, the 1994 National Institutes of Health (NIH) Human Embryo Research Panel permitted the creation of human embryos for research.⁶¹ However, the report contrasted conception via fertilization with concep-

tion via nuclear transfer, suggesting that the latter would be more acceptable because “no fertilization of male and female gametes would be involved.”⁶¹ However, concern for the moral symbolism of human ontogeny is based on the potential of an embryo, not its method of creation. As a result, the panel’s recommendations were controversial and resulted in a presidential directive and 1996 federal law that banned federal funding for “the creation of a human embryo or embryos for research purposes.”⁶² This, in turn, led the NIH to propose a controversial distinction between “derivation” and “use” of human embryonic stem cells to justify funding research for the latter, but not the former, activity.⁶³ Under this policy, and within strict guidelines, the use of stem cells lines that have already been created by privately supported (rather than publicly funded) sources is permitted. In every case, cells must derive only from fertilized embryos that would otherwise be discarded after in vitro fertilization treatment or from already aborted fetuses. Donors must be aware of the use of these embryonic cells and that compensation is prohibited.

The net effect of this cascade of policy making has been to take the ethical issues of creating human embryos off the table of detailed public discussion. Two subsequent important policy reports, from the American Association for the Advancement of Science⁶⁴ and the National Bioethics Advisory Commission,⁶⁵ have taken advantage of this shifted focus and avoided the issue of the source of stem cells altogether. Although politically safer, it still leaves the ethical issues involved in therapeutic cloning unaddressed and the field open to polarized views. Legislative approaches can never obviate the ethical problems implicit in public funding but, with broad public discussion, public policy can better reflect a respect for both the sincere ethical opinions of the compelled minority against the compelling majority and perceived public needs.

Conclusion

The ethics of embryonic stem cell use are complex and deeply personal, but many of the ethical challenges posed by stem cell research would become transient if nonembryonic cell sources are developed. For those who invest embryos with all the rights and interests of persons, the use of embryonic stem cells will always be difficult to accept, for reasons that biology alone can neither address nor adjudicate. For those who accept a developmental view of human moral status, hard questions still arise regarding the respect due the human embryo, which must be balanced against the needs of living patients and collateral ethical effects of prohibition. Even those who give no moral standing to early human embryos share a universal social interest in avoiding an inappropriate polarization of the public dialogue. While nonembryonic cell sources may make these arguments moot, the ethical issues remain pertinent until such sources are available. The ethical discussions need to be advanced carefully and openly to avoid an untimely political truncation

of the potential of this research and with a clear eye toward its ultimate social, legal, and ethical impacts.

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Only one rule in medical ethics needs concern you—
that action on your part which best conserves the interests of your patient.

—Martin H. Fischer (1879-1962)