

7.3.8 Research with Stem Cells

Human stem cells are widely seen as offering a source of potential treatment for a range of diseases and are thus the subject of much research. Clinical studies have validated the use of adult stem cells in a limited number of therapies, but have yet to confirm the utility of embryonic stem cells.

Physicians who conduct research using stem cells obtained from any source (established tissue, umbilical cord blood, or embryos) must, at a minimum:

- (a) Adhere to institutional review board (IRB) requirements.
- (b) Ensure that the research is carried out with appropriate oversight and monitoring.
- (c) Ensure that the research is carried out with appropriate informed consent. In addition to disclosure of research risks and potential benefits, at minimum, the consent disclosure should address:
 - (i) for a donor of cells to be used in stem cell research:
 - a the process by which stem cells will be obtained;
 - b what specifically will be done with the stem cells;
 - c whether an immortal cell line will result; and
 - d the primary and anticipated secondary uses of donated embryos and/or derived stem cells, including potential commercial uses.
 - (ii) for a recipient of stem cells in clinical research:
 - a the types of tissue from which the stem cells derive (e.g., established tissue, umbilical cord blood, or embryos); and
 - b unique risks posed by investigational stem cell products (when applicable), such as tumorigenesis, immunological reactions, unpredictable behavior of cells, and unknown long-term health effects.

The professional community as well as the public remains divided about the use of embryonic stem cells for either research or therapeutic purposes. The conflict regarding research with embryonic stem cells centers on the moral status of embryos, a question that divides ethical opinion and that cannot be resolved by medical science. Regardless whether they are obtained from embryos donated by individuals or couples undergoing in vitro fertilization, or from cloned embryos created by somatic cell nuclear transfer (SCNT), use of embryonic stem cells currently requires the destruction of the human embryo from which the stem cells derive.

The pluralism of moral visions that underlies this debate must be respected. Participation in research involving embryonic stem cells requires respect for embryos, research participants, donors, and recipients. Embryonic stem cell research does not violate the ethical standards of the profession. Every physician remains free to decide whether to participate in stem cell research or to use its products. Physicians should continue to be guided by their commitment to the welfare of patients and the advancement of medical science.

Physicians who conduct research using embryonic stem cells should be able to justify greater risks for subjects, and the greater respect due embryos than stem cells from other sources, based on expectations that the research offers substantial promise of contributing significantly to scientific or therapeutic knowledge.

AMA Principles of Medical Ethics: V

Background report(s):

CEJA Report 5-A-11 Amendment to Opinion E-2.146, Cloning for biomedical research

CEJA Report 7-A-03 Cloning for biomedical research

CEJA Report 2-A-99 The ethics of human cloning

REPORT OF THE COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS¹

CEJA Report 5-A-11

Subject: Amendment to Opinion E-2.146, “Cloning for Biomedical Research”

Presented by: John W. McMahon, Sr., MD, Chair

Referred to: Reference Committee on Amendments to Constitution and Bylaws
(Patricia L. Austin, MD, Chair)

1 Organized Medical Staff Section (OMSS) Resolutions 1, “AMA Opposition to Embryonic Stem
2 Cell Research,” and 15, “Stem Cell Research,” were referred to the OMSS Governing Council
3 (GC) for deliberation at the 2009 Annual Meeting. The OMSS GC believed that these issues
4 would be most appropriately addressed by the Council on Ethical and Judicial Affairs (CEJA).
5

6 Both resolutions asked the American Medical Association (AMA) to support specific positions on
7 stem cell research. OMSS Resolution 1 asked that the AMA promote the scientific truth that an
8 embryo is not property but rather is a human being with all the attendant rights; not support
9 embryonic stem cell research as it results in the termination of human life; seek legislative support
10 to restore Executive Order 13455, which was revoked by the current Administration; oppose
11 therapeutic cloning as a way of producing embryonic stem cells with a predetermined genetic
12 patrimony in order to overcome the problem of immune system rejection; and oppose the use of
13 stem cells for selecting the genetic characteristics of offspring.
14

15 OMSS Resolution 15 asks that the AMA support President Obama in his consideration of: the
16 ethical issues relating to embryonic cell research; policy to restrict federal funding of research
17 involving human cloning; policy to restrict federal funding of stem cell research that creates human
18 embryos for the sole purpose of research.
19

20 The Council reviewed the resolutions along with AMA’s related ethics policy, most relevant being
21 Opinion E-2.146 (AMA Policy Database), “Cloning for Biomedical Research.” CEJA concluded
22 that in order to respond to both resolutions, the Opinion needed clarification and updating to reflect
23 the current state of scientific research.
24

25 AMA POLICY

26
27 The AMA has House of Delegates policy on stem cell research. Policy H-460.915, “Cloning and
28 Stem Cell Research,” states that the AMA: (1) supports biomedical research on multipotent stem
29 cells (including adult and cord blood stem cells); (2) supports the use of somatic cell nuclear
30 transfer technology in biomedical research (therapeutic cloning); (3) opposes the use of somatic
31 cell nuclear transfer technology for the specific purpose of producing a human child (reproductive

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1 cloning); (4) encourages strong public support of federal funding for research involving human
2 pluripotent stem cells; and (5) will continue to monitor developments in stem cell research and the
3 use of somatic cell nuclear transfer technology.[1]
4

5 *Policy Related to Stem Cell Research*

6

7 In its 2003 report on cloning for biomedical research, CEJA noted that:

8
9 Different types of recommendations have been made to restrict research on stem cells from
10 cloned human embryos. Some have asked that stem cell research be restricted to less
11 controversial sources, such as adult stem cells, which have shown increasing promise. They
12 maintain that these limits would put an end to the unjustified destruction of early forms of
13 human life. For example, a majority on the President's Council on Bioethics (PCB)
14 recommended a moratorium on research on stem cells derived from cloned human embryos. In
15 the absence of specific criteria that would result in the lifting of the moratorium, this proposed
16 suspension of research has been likened to a recommendation for a ban.
17

18 Others maintain that research using stem cells derived from cloned embryos should be
19 undertaken only if no less controversial approach exists that is equally promising. In fact,
20 given the technical difficulties that somatic cell nuclear transfer (SCNT) presents, this
21 restriction already is a reality of laboratory life. The scientific community is using SCNT to
22 produce embryos only for research identified as uniquely promising.
23

24 Several governmental bodies, including the National Bioethics Advisory Commission (NBAC)
25 and the 1994 National Institutes of Health Human Embryo Research Panel (HERP) have
26 proposed restrictions on federal funding of research on stem cells from human embryos
27 deliberately created for research, including those created through SCNT. However, these
28 restrictions would not prohibit the research itself, which could be undertaken in the private
29 sector. In fact, NBAC's recommendation was to be reconsidered if research in the private
30 sector showed great promise.
31

32 It is important to acknowledge that the recommendations of HERP, NBAC, and the PCB were
33 never enacted into law and have been used only for advisory purposes.
34

35 In August 2001, President Bush announced a decision to limit federal funding to research on
36 approximately 60 genetically diverse embryonic stem cell lines already in existence in the
37 federal registry, which excludes any lines that were derived with private funds. In fact,
38 currently only nine cell lines currently meet the eligibility criteria for federally funded research
39 and are available to scientists. In addition, all of them were exposed to mouse feeder cells as
40 part of the cultivation process, raising some of the same ethical issues as xenotransplantation.
41 Finally, under the President's decision, federal funds could not be used to further any of the
42 uniquely promising goals of cloning-for-biomedical-research.[2]
43

44 FEDERAL & STATE POLICY

45

46 Federal regulations regarding research with embryonic stem cells are currently in flux. On March
47 9, 2009, President Barack Obama issued Executive Order (EO) 13505, "Removing Barriers to
48 Responsible Scientific Research Involving Human Stem Cells," which revoked President Bush's
49 August 2001 policy.[3] EO 13505 and the subsequently released NIH Guidelines for Human Stem

1 Cell Research allowed for federal funding of research on newly created stem cell lines.[4]
2 However, the other three components of the Bush policy remained intact: a cell line may be derived
3 only from an embryo left over from the in vitro fertilization (IVF) process, there must be no
4 financial inducements in obtaining the embryo, and informed consent must be obtained from the
5 embryo donor. Some in the scientific community are concerned that continuing to restrict federal
6 funding to lines created from donated embryos left over from infertility treatment significantly
7 impedes research, given that there are other significant sources of embryos that could be used to
8 establish disease-specific stem cell lines: parthenogenesis, SCNT, and embryos created through
9 IVF specifically for research.[4] On August 22, 2010, the Federal District Court for the District of
10 Columbia issued a temporary injunction halting federal spending for research involving embryonic
11 stem cells in a lawsuit alleging that EO 13505 made it more difficult for researchers using adult
12 stem cells to compete for federal research grants.[5]

13

14 State laws vary widely with regard to their stance on research with embryonic stem cells. The
15 primary sources for embryonic stem cells are existing stem cell lines, aborted or miscarried
16 embryos, embryos left over from in vitro fertilization, and cloned embryos. Individual states may
17 permit or restrict research on cells from each of these sources.[3]

18

19 Whereas eight states have statutes that promote stem cell research, one state, South Dakota, forbids
20 research on any embryo regardless of the origin. Likewise many states restrict research on aborted
21 fetuses or embryos and half restrict their sale.[3] Louisiana is the only state that banned research
22 on IVF embryos; five states prohibit research on cloned embryos. Several states limit the use of
23 state funds for identified aspects of stem cell research, though more states have specifically
24 authorized funding for such research.[3]

25

26 STATE OF THE SCIENCE

27

28 The National Institutes of Health defines stem cells as “cells with the ability to divide for indefinite
29 periods in culture and to give rise to specialized cells.”[6] There are two major categories of stem
30 cells, adult stem cells and embryonic stem cells. Adult stem cells are sometimes referred to as
31 nonembryonic stem cells and are “a relatively rare undifferentiated cell found in many organs and
32 differentiated tissues with a limited capacity for both self renewal (in the laboratory) and
33 differentiation. Such cells vary in their differentiation capacity, but it is usually limited to cell
34 types in the organ of origin. This is an active area of investigation.”[6] Cord blood and some fetal
35 tissues also contain adult stem cells.

36

37 *Adult Stem Cells*

38

39 Bone marrow (which contains a type of adult stem cells) has been in clinical use for over 40 years,
40 mostly transplanted to treat blood disorders.[7] Similarly, cord blood stem cells have been used for
41 the past 15–20 years.[7]

42

43 Although research with adult stem cells dates back to the 1950s, there continues to be debate in
44 scientific community over the capabilities and limitations of these types of stem cells, particularly
45 if stem cells found in one tissue can give rise to cell types in different tissue. There has been
46 disagreement whether embryonic stem cells may have clinical advantages over adult stem cells;
47 however, in recent years scientists working with adult stem cells have acknowledged that adult
48 stem cells had limitations and could not replace embryonic stem cells in all situations.[8]

1 Clinical trials have explored using adult stem cells to treat ischemic heart disease, spinal cord
2 lesions, nonunion of fractured bones, Parkinson’s disease, Huntington’s disease, and type 1
3 diabetes, among other conditions.[7] Although some trials have yielded promising results, it will
4 likely be several years before adult stem cells will be utilized in these clinical settings.

5
6 In 2007, scientists identified techniques that would allow some specialized adult human cells to be
7 genetically reprogrammed to assume a stem-cell-like state. Although these “induced pluripotent
8 stem cells” (iPSCs) meet the defining criteria for pluripotent stem cells, the NIH notes that “it is
9 not known [whether] iPSCs and embryonic stem cells differ in clinically significant ways.”[9]
10 While iPSCs have already become important tools in drug development and disease modeling, it
11 will be years before they can be used therapeutically. Current techniques for inducing pluripotency
12 require integration of foreign DNA, and thus transplantation of iPSCs into humans is currently not
13 possible.[10]

14 15 *Embryonic Stem Cells*

16
17 The second major category of stem cells is that of embryonic stem cells. Whereas research and
18 therapy using adult stem cells has a proven track record, that is not the case with embryonic stem
19 cells, for which bench and clinical science lags by decades. Embryonic stem cells are defined by
20 the NIH as “undifferentiated cells derived from a 5-day preimplantation embryo that are capable of
21 dividing without differentiating for a prolonged period in culture, and are known to develop into
22 cells and tissues of the three primary germ layers.”[6] Embryonic stem cells are thought to have
23 the greatest clinical application due to their ability to differentiate and regenerate.[7,8]

24
25 The first embryonic stem cell line was established in 1998 and the first-ever human trial of a
26 medical treatment derived from embryonic stem cells was approved in the United States in 2009
27 for research into the treatment of spinal cord injuries.[7,11] Potential risks are great and include
28 spontaneous and uncontrolled cellular differentiation, tumorigenesis and the potential for
29 transmission of genetic abnormalities.[8] Other risks include immunological reaction or rejection,
30 unpredictable cell behavior, and unknown long-term health effects.[12] Although clinical trials are
31 underway to examine tolerability of therapy using embryonic stem cells, if these trials are
32 successful it will likely be many more years before therapies are available outside of the research
33 setting.[13]

34 35 ETHICAL ISSUES

36
37 Ethical concern has often focused solely on the source of stem cells. Much of the controversy
38 surrounding biomedical research with stem cells is generated by the use of human embryonic stem
39 cells and the plurality of views in our society regarding the moral status of early embryos. Concern
40 is exacerbated by the fact the current techniques for retrieving stem cells require that the embryo be
41 disaggregated or destroyed. This question of moral status cannot be answered by science and
42 decades of moral debate have not yielded consensus.

43
44 Whether it is ethical to create embryos for research purposes by means of IVF or SCNT has also
45 been hotly debated. SCNT, also known as cloning-for-biologic-research, involves introducing
46 nuclear material from a somatic cell into an enucleated oocyte. This process yields an embryo that
47 is genetically nearly identical to the donor of the somatic cell: its nuclear DNA is contributed by
48 the nucleus donor, while its cytoplasmic DNA is contributed by the oocyte donor. Current NIH
49 guidelines restrict research to the use of stem cells derived from donated surplus IVF embryos.

1 Even absent the NIH guidelines, the availability of cloned embryos as sources of stem cells is
2 constrained by the fact that to date human embryos have not been derived through SCNT due to
3 difficulties in initiating human embryo development. Moreover it has been difficult to convince
4 women to undergo the process of oocyte donation, with its associated dangers, discomforts, and
5 psychosocial risks, without compensation. At present, the National Academy of Sciences
6 recommends against compensating egg donors and two states have outlawed the practice. One
7 state, however, allows compensation commensurate with what a woman would receive for
8 donating eggs for IVF in treatment of infertility.[3]
9

10 The use of adult stem cells and induced pluripotent stem cells derived from somatic cells does not
11 pose questions about the moral status of the embryo. However, stem cell research poses other
12 ethical challenges, regardless of the source of stem cells. As with any research involving human
13 biological materials, stem cell research requires a robust process of informed consent. The
14 emerging consensus about the core components of consent for research with biological specimens
15 requires that donors be informed about the specific procedures involved and their risks; what will
16 be done with the biological specimen—in the case of stem cell research; whether an embryo will be
17 created and then destroyed, the intention to derive immortal cell lines for subsequent use in
18 research and, possibly, therapeutic contexts; and primary and secondary uses (when known) of
19 specimens. Informed consent should also address donors' rights to restrict use of their biological
20 materials to only specified purposes, what will happen should they withdraw their consent,
21 potential recontact, and donors' "reach through" rights with respect to commercial products that
22 may be developed through use of their biological materials.[12]
23

24 Clinical research involving stem cells poses further ethical challenges. As noted above, questions
25 remain about the safety of therapeutic uses of stem cells or stem cell products, particularly
26 embryonic stem cells. Risks include spontaneous and uncontrolled cell differentiation and
27 tumorigenesis and immunological reactions or tissue rejection, the severity and likelihood of which
28 are uncertain, as well as potential unknown long-term health effects.[12]
29

30 RECOMMENDATION

31
32 The Council on Ethical and Judicial Affairs recommends that Opinion E-2.146, "Cloning for
33 Biomedical Research" (Appendix) be amended by substitution as follows and that the remainder of
34 this report be filed:
35

36 Opinion 2.146 – Research with Stem Cells

37
38 Human stem cells are widely seen as offering a source of potential treatment for a range of
39 diseases and are thus the subject of much research. Clinical studies have validated the use of
40 adult stem cells in a limited number of therapies, but have yet to confirm the utility of
41 embryonic stem cells.
42

43 Physicians who conduct research using stem cells obtained from any source (established tissue,
44 umbilical cord blood, or embryos) must, at a minimum:
45

- 46 (a) adhere to institutional review board (IRB) requirements;
- 47
- 48 (b) ensure that the research is carried out with appropriate oversight and monitoring; and

1 (c) ensure that the research is carried out with appropriate informed consent. In addition to
2 disclosure of research risks and potential benefits, at minimum, the consent disclosure
3 should address:

4
5 (i) for a donor of cells to be used in stem cell research:

6
7 (a) the process by which stem cells will be obtained;

8
9 (b) what specifically will be done with the stem cells;

10
11 (c) whether an immortal cell line will result; and

12
13 (d) the primary and anticipated secondary uses of donated embryos and/or derived stem
14 cells, including potential commercial uses.

15
16 (ii) for a recipient of stem cells in clinical research:

17
18 (a) the types of tissue from which the stem cells derive (e.g., established tissue,
19 umbilical cord blood, or embryos); and

20
21 (b) unique risks posed by investigational stem cell products (when applicable), such as
22 tumorigenesis, immunological reactions, unpredictable behavior of cells, and
23 unknown long-term health effects.

24
25 The professional community as well as the public remains divided about the use of embryonic
26 stem cells for either research or therapeutic purposes. The conflict regarding research with
27 embryonic stem cells centers on the moral status of embryos, a question that divides ethical
28 opinion and that cannot be resolved by medical science. Regardless whether they are obtained
29 from embryos donated by individuals or couples undergoing in vitro fertilization, or from
30 cloned embryos created by somatic cell nuclear transfer (SCNT), use of embryonic stem cells
31 currently requires the destruction of the human embryo from which the stem cells derive.

32
33 The pluralism of moral visions that underlies this debate must be respected. Participation in
34 research involving embryonic stem cells requires respect for embryos, research participants,
35 donors, and recipients. Embryonic stem cell research does not violate the ethical standards of
36 the profession. Every physician remains free to decide whether to participate in stem cell
37 research or to use its products. Physicians should continue to be guided by their commitment to
38 the welfare of patients and the advancement of medical science.

39
40 Physicians who conduct research using embryonic stem cells should be able to justify greater
41 risks for subjects, and the greater respect due embryos than stem cells from other sources, based
42 on expectations that the research offers substantial promise of contributing significantly to
43 scientific or therapeutic knowledge.

44
45 (Modify HOD/CEJA Policy)

Fiscal Note: Staff cost estimated at less than \$500 to implement.

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APPENDIX

E-2.146 Cloning for Biomedical Research

Stem cells derived from cloned human embryos resulting from somatic cell nuclear transfer technology are promising as a potential source of treatment in a wide range of diseases. However, much controversy arises from the necessity to destroy embryos in order to extract their stem cells for use in biomedical research. The conflict centers on the moral status of embryos, a question that divides ethical opinion and that cannot be resolved by medical science.

- (1) While the pluralism of moral visions that underlie this debate must be respected, physicians collectively must continue to be guided by their paramount obligation to the welfare of their patients. In this light, cloning-for-biomedical-research is consistent with medical ethics. Every physician remains free to decide whether to participate in stem cell research or to use its products.
- (2) Cloning-for-biomedical-research requires appropriate oversight and monitoring. At a minimum, not only is the oversight of an institutional review board required, but also that of a regulatory body, such as the Office for Human Research Protections, to monitor progress in the field, assist in developing relevant guidelines, and ensure that the technique of cloning-for-biomedical-research is used only if uniquely promising.
- (3) Informed consent by subjects participating in cloning-for-biomedical-research is governed by standard principles: voluntary participation and disclosure of all relevant risks and benefits to subjects. Disclosure to the donor of the oocyte and the donor of the somatic cell also must include:
 - (a) Description of the procurement procedures specific to the donor
 - (b) Statement of the intention to create a cloned human embryo through introduction of the somatic cell's nucleus into the enucleated egg for research purposes (and not for transfer to a woman's uterus)
 - (c) Acknowledgment that the extraction of stem cells will require the cloned embryo's destruction
 - (d) The intention to derive immortal cell lines from the stem cells to be used in research and possibly in therapeutic contexts; primary and secondary uses should be disclosed and individuals should be free to refuse the use of their biological materials for specified purposes
 - (e) Potential commercial uses and patent or ownership issues (as described in Opinion E-2.08, "Commercial Use of Human Tissue")
- (4) The informed consent process for potential recipients of stem cells derived from cloned embryos should conform with ethical standards outlined in the Council on Ethical and Judicial

Affairs' Opinion E-2.07, "Clinical Investigation," and address additional disclosures including provenance of stem cells.

- (5) Due to the possibilities of contamination by infectious agents from other species and damage to DNA during growth of new tissues and organs, products of cloning-for-biomedical-research raise ethical concerns similar to those surrounding xenotransplantation. Therefore, the informed consent process for potential recipients of these products also should conform to Opinion E-2.169, "The Ethical Implications of Xenotransplantation." (V)

Issued December 2003 based on the report "Cloning-for-Biomedical-Research," adopted June 2003.

REPORT OF THE COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS*

CEJA Report 7 – A-03

Subject: Cloning-for-Biomedical-Research

Presented by: Leonard J. Morse, MD, Chair

Referred to: Reference Committee on Amendments to Constitution
and Bylaws
(Donna A. Woodson, MD, Chair)

1 In July 2002, the President’s Council on Bioethics (PCB), created by executive order of George W.
2 Bush, issued its first report: “Human Cloning and Human Dignity: An Ethical Inquiry.”¹ The topic
3 of human cloning had been and continues to be featured regularly in the professional and lay press
4 for the scientific promise and moral quandaries it presents. It also has captured the attention of
5 legislators. At this time, it is important that organized medicine offer guidance to physicians as to
6 how they should proceed from the viewpoint of professional ethics because various interventions
7 made possible by human cloning are likely to rely on physicians’ expertise and could have an
8 impact on their clinical activities.

9 10 TERMINOLOGY AND SCOPE

11
12 Cloning is a term used to describe the asexual production of a new organism through somatic cell
13 nuclear transfer (SCNT), which involves the introduction of the nuclear material of a somatic cell
14 into an enucleated oocyte. This process yields an embryo that is genetically virtually identical to
15 the donor of the somatic cell; that is, its nuclear DNA is contributed by the nucleus donor, while its
16 cytoplasmic DNA is contributed by the oocyte donor.

17
18 If the cell resulting from the transfer of a human somatic nucleus to an enucleated oocyte by SCNT
19 technology were to divide and develop successfully, the product would lead to a cloned human
20 embryo. In theory, if such an embryo were implanted in a woman’s uterus and the ensuing
21 pregnancy carried to term, the resulting child would be genetically virtually identical to the donor
22 of the somatic cell. The President’s Council on Bioethics has referred to this activity as “cloning-
23 to-produce-children.” In contrast, the process of producing cloned human embryos from SCNT
24 with the intent to extract their stem cells for use in medical research has been termed “cloning-for-
25 biomedical-research.”²

26
27 Stem cell research has received increasing attention because of the potential benefit it holds for
28 patients (See Council on Scientific Affairs (CSA) Report). This report of the Council on Ethical

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1 and Judicial Affairs (CEJA) specifically considers the ethical appropriateness of using embryonic
2 stem cells in biomedical research, particularly where stem cells are derived from human embryos
3 created through SCNT technology.

4
5 This report does not expand on broad ethical considerations raised by possible long-term
6 consequences of all stem cell research, such as the evolution of our concepts of aging and
7 mortality, or of personal identity and bodily integrity if we acquired the ability to replace and
8 regenerate bodily tissues and organs.³

9 10 STATUS OF THE HUMAN EMBRYO

11
12 Much of the controversy surrounding biomedical research on embryonic stem cells in general
13 arises from the plurality of views within our society regarding the moral worth of early embryos,
14 particularly because the retrieval of stem cells necessitates the embryo's disaggregation or
15 destruction. The various moral perspectives give rise to incompatible notions of how much respect
16 is owed to and what rights are possessed by preimplantation human embryos at the blastocyst
17 stage.

18
19 Those who believe that an embryo at any stage possesses the same moral status and rights as a
20 mature person will be opposed to destruction of an embryo for any reason. For others, though
21 respect for the blastocyst may symbolize a commitment to life, it does not have full moral status in
22 the absence of a nervous system and differentiated organs. Therefore, some adhering to this view
23 believe that biomedical research on embryonic stem cells should be permitted out of respect and
24 concern for living persons, because of the research's potential to yield medical advances that will
25 help treat disease, improve the quality of life of patients, and save lives. Others would require a
26 compelling argument for using embryonic stem cells instead of other types of stem cells.⁴

27
28 Cast in these terms, the debate over embryonic stem cell research seems to focus on the moral
29 worth of an embryo at the blastocyst stage rather than on the method through which the embryo is
30 created.⁵ From a professional perspective that relies on the *Principles of Medical Ethics*, a strong
31 argument can be made that physicians' professional obligation to living individuals overrides their
32 obligation to the earliest forms of life. As noted by the American College of Obstetricians and
33 Gynecologists, in its Committee Opinion on "Preembryo Research," the preimplantation embryo,
34 at less than 14 days, does not possess the biologic individuality necessary for a concrete
35 potentiality to become a human person. With its individuality not yet determined (an embryo at
36 this stage could divide naturally to form twins, for example), the blastocyst should not be attributed
37 the same worth as a human person.⁶

38
39 In connection with the general debate on the moral status of the embryo, some draw moral
40 distinctions based on the intended use of the embryos – embryos created in the context of IVF to
41 assist couples in conceiving and those created solely for the purpose of research. It is also
42 important to note that some embryos created for uterine implantation are not used for this purpose
43 because they are no longer needed (supernumerary embryos), and therefore are often discarded or
44 are used for research.

1 Only embryos intentionally created for biomedical research are, from their inception, lacking in the
2 potentiality to become a human being and therefore not due the corresponding respect.⁷ Some
3 maintain that such embryos are “instrumentalized” or treated as though they were objects, in a way
4 that disrespects human life. Others look at the same facts and conclude that because no future life
5 was intended from the outset, there are no future interests of a human life to be harmed, so the
6 process is morally less problematic. Finally, some have argued that it is no worse to destroy a
7 blastocyst intended from the start for biomedical research by extracting the stem cells from its inner
8 mass than to discard a frozen embryo.⁴

9 10 *Cloned Embryos*

11
12 Similar to the concerns discussed above, it appears that some of the resistance toward the use of
13 stem cells from embryos created through SCNT technology arises from confusion between
14 cloning-to-produce children and cloning-for-biomedical-research. Technically, both these
15 activities would rely on the same baseline technology, SCNT; however, it would be used toward
16 fundamentally different goals.⁸ Other reasons for which cloning-for-biomedical-research has been
17 opposed include fear that the research might lead to new forms of the “instrumentalization” of life,
18 or using embryos as mere means to an end. If cloned embryos are regarded as disposable
19 commodities, then scientists might mass-produce them.

20
21 Another objection is that cloning-for-biomedical-research may open the door to cloning-to-produce
22 children.⁸ Even though scientists involved in stem cell research may have no intention of exploring
23 the possibility of transferring a cloned embryo into a woman’s uterus with the goal of a resulting
24 pregnancy, it is argued that they are helping to improve the technique of SCNT, so that it may
25 become possible for a cloned embryo to develop to the stage where it could be implanted
26 successfully. However, given the low success rates and high safety concerns associated with the
27 cloning of mammals, and repeated failed attempts to create a primate through SCNT technology,
28 there is little reason to expect that human beings would succeed in producing cloned children using
29 this technology.⁹ At this time, cloning-to-produce-children appears impossible. Therefore, it is
30 inaccurate to claim that cloned human embryos have the potentiality for human life. Fears related
31 to cloning-to-produce children may offer a compelling argument for effective protections against
32 certain uses of cloned embryos, but they do not justify the prohibition of all cloning.

33 34 POLICY RELATED TO CLONING-FOR-BIOMEDICAL-RESEARCH

35 36 *Restricting Embryonic Stem Cell Research*

37
38 Different types of recommendations have been made to restrict research on stem cells from cloned
39 human embryos. Some have asked that stem cell research be restricted to less controversial
40 sources, such as adult stem cells, which have shown increasing promise. They maintain that these
41 limits would put an end to the unjustified destruction of early forms of human life. For example, a
42 majority on the PCB recommended a moratorium on research on stem cells derived from cloned
43 human embryos. In the absence of specific criteria that would result in the lifting of the
44 moratorium, this proposed suspension of research has been likened to a recommendation for a ban.

1 Others maintain that research using stem cells derived from cloned embryos should be undertaken
2 only if no less controversial approach exists that is equally promising.⁴ In fact, given the technical
3 difficulties that SCNT presents, this restriction already is a reality of laboratory life. The scientific
4 community is using SCNT to produce embryos only for research identified as uniquely promising.
5 Several governmental bodies, including the National Bioethics Advisory Commission (NBAC) and
6 the 1994 National Institutes of Health Human Embryo Research Panel (HERP) have proposed
7 restrictions on federal funding of research on stem cells from human embryos deliberately created
8 for research, including those created through SCNT.^{10, 11} However, these restrictions would not
9 prohibit the research itself, which could be undertaken in the private sector. In fact, NBAC's
10 recommendation was to be reconsidered if research in the private sector showed great promise.

11
12 It is important to acknowledge that the recommendations of HERP, NBAC, and the PCB were
13 never enacted into law and have been used only for advisory purposes.

14
15 In August 2001, President Bush announced a decision to limit federal funding to research on
16 approximately 60 genetically diverse embryonic stem cell lines already in existence in the federal
17 registry, which excludes any lines that were derived with private funds.¹² In fact, currently only
18 nine cell lines currently meet the eligibility criteria for federally funded research and are available
19 to scientists.¹³ In addition, all of them were exposed to mouse feeder cells as part of the cultivation
20 process, raising some of the same ethical issues as xenotransplantation.^{14, 15} Finally, under the
21 President's decision, federal funds could not be used to further any of the uniquely promising goals
22 of cloning-for-biomedical-research.

23
24 *Justifications for Research on Stem Cells Derived from Cloned Human Embryos*

25
26 Proponents of embryonic stem cell research base their arguments on its potentially powerful
27 contributions to treating human disease and disability. Many scientists, for example, take the view
28 that benefits from this form of research are likely to be so great that it must be allowed to proceed.⁷
29 This is reflected in the respective reports on stem cell research of the American Association for the
30 Advancement and Institute for Civil Liberties, as well as the Committee on the Biological and
31 Biomedical Application of Stem of Science, Board on Life Sciences, National Research Council,
32 Board on Neuroscience and Behavioral Health, Institute of Medicine, all of which are supportive
33 of continued research on embryonic stem cells.^{16, 17} Some argue that prohibiting this research
34 would be more disrespectful of human life than the destruction of embryos it entails. At least, they
35 argue that embryonic stem cell research should be pursued along with other stem cell research,
36 until it becomes known whether one is more promising or whether perhaps the different types of
37 research offer distinct possibilities.^{16, 18}

38
39 If the promise of stem cell research is realized with regard to renewable sources of cells
40 replacement, gene therapy or tissue and organ transplantation, cloning-for-biomedical-research
41 could prove uniquely promising. It could lead to the growth of tissues or organs that are
42 immunologically compatible with the individual in need, removing the most important barrier to
43 successful transplantation. This is addressed in the CSA Report, as is the unique opportunity that
44 research on stem cells derived from cloned human embryos provides to understand molecular and
45 cellular events underlying human diseases.¹⁷

1 EMBRYONIC STEM CELL RESEARCH: A VIEW FROM ORGANIZED MEDICINE

2
3 By examining the ethical considerations this research raises, organized medicine can advocate
4 responsible conduct of research to the medical community. As an issue that is based on moral
5 values and matters of personal conscience rather than scientific discourse, the moral status of the
6 embryo cannot be settled by organized medicine. This is not to say that investigators should
7 proceed with cloning-for-biomedical-research with no regard for ethics, but rather that professional
8 standards of ethics should guide the process.

9
10 *Relevant AMA Policies*

11
12 Research on stem cells derived from cloned embryos offers possibilities for medical advancement
13 that could save lives, improve quality of life, and alleviate suffering. It is consistent with principles
14 of medical ethics, particularly physicians' paramount obligation to the welfare of their patients
15 (Principle VIII) and their responsibility to advance scientific knowledge (Principle V).¹⁹ Therefore
16 from the standpoint of medical professionalism, physicians may participate in and support cloning
17 for biomedical research, so long as they proceed in accordance with adequate research ethics
18 standards and with the law. Individual physicians remain free to decide whether to participate in
19 stem cell research or to use its products.

20
21 An important methodological approach in bioethics is to compare and contrast the new ethical
22 dilemmas technological advances create to established standards, in an effort to begin to resolve
23 them. A similar exercise, relying on existing policies in the *Code of Medical Ethics*, may help
24 clarify physicians' ethical responsibilities in relation to SCNT.

25
26 Opinion E-2.14, "In Vitro Fertilization"²⁰ is unambiguous in its support of IVF to assist couples
27 reproduce. Specifically, the *Code* is clear that producing embryos to assist child bearing is
28 ethically acceptable. The opinion also allows fertilized ova no longer intended for implantation to
29 be used in research, if certain ethical safeguards are respected. Overall, the opinion acknowledges
30 the usefulness of IVF in contributing to medicine's understanding of how genetic defects are
31 transmitted and how they might be prevented or treated. Similarly, Opinion E-2.141, "Frozen Pre-
32 embryos,"²¹ states that "research on pre-embryos should be permitted as long as the pre-embryos
33 are not destined for transfer to a woman for implantation and as long as the research is conducted
34 [ethically]."

35
36 While the *Code* in its current form supports research on supernumerary embryos, it has not offered
37 a systematic ethical analysis of embryos created expressly for the purpose of conducting
38 biomedical research or of cloned human embryos produced for biomedical research.

39
40 THE NEED FOR APPROPRIATE SAFEGUARDS IN CLONING-FOR-BIOMEDICAL-
41 RESEARCH

42
43 Medical science cannot settle all the ethical quandaries that surround cloning-for-biomedical-
44 research and divide our society. However, organized medicine can join those who recommend

1 special safeguards to protect research subjects. In addition to such safeguards, continuing oversight
2 and monitoring of findings will be needed.

3
4 *Informed Consent*

5
6 Prior to producing an embryo through SCNT technology for research purposes, specific consent
7 must be obtained from at least two categories of subjects, the egg donor and the somatic cell donor.
8 Beyond customary information regarding relevant risks and benefits to subjects, disclosure to each
9 donor must include:

- 10
- 11 • description of the procurement procedures specific to the donor;
 - 12 • statement of the intention to create a cloned human embryo through introduction of the
13 somatic cell's nucleus into the enucleated egg for research purposes (and not for transfer to
14 a woman's uterus);
 - 15 • acknowledgment that the extraction of stem cells will require the cloned embryo's
16 destruction;
 - 17 • the intention to derive immortal cell lines from the stem cells to be used in research and
18 possibly in therapeutic contexts; primary and secondary uses should be disclosed and
19 individuals should be free to refuse the use of their biological materials for specified
20 purposes;
 - 21 • potential commercial uses and patent or ownership issues (as described in Opinion E-2.08,
22 "Commercial Use of Human Tissue").²²
- 23

24 The informed consent process for potential recipients of stem cells derived from cloned embryos
25 should conform with ethical standards outlined in CEJA's Opinion E-2.07, "Clinical
26 Investigation"²³ and address additional disclosures regarding provenance of stem cells and ethical
27 considerations associated with xenotransplantation, as outlined in Opinion E-2.169, "The Ethical
28 Implications of Xenotransplantation."¹⁵

29
30 *Research Oversight*

31
32 Currently, federal funds cannot be used to create embryos solely intended for research purposes or
33 to conduct research that entails the destruction or discarding of human embryo. However, this does
34 not mean that there exists no federal oversight mechanism to regulate and monitor cloning-for-
35 biomedical research. Indeed, when tissue transplantation is the endpoint, every step of cloned
36 human embryo stem cell research is subject to regulation of cell-based therapies by the Food and
37 Drug Administration (FDA). However, if SCNT research has objectives other than transplantation,
38 researchers in the private sector are left without a clear set of regulatory guidelines.⁴ As described
39 in Opinion E-2.07, "Clinical Investigation," the scientific validity and the ethical considerations
40 raised by any research should be carefully assessed and given due weight by qualified bodies such
41 as institutional review boards.²³ Because research on stem cells extracted from cloned human
42 embryos raises unique social concerns that are not addressed in general guidelines that govern the
43 conduct of research, the Office for Human Research Protection or other similar entity should help
44 monitor progress in the field and assist in developing relevant guidelines.

1 RECOMMENDATIONS

2
3 The Council recommends that the following be adopted and the remainder of this report be filed:

4
5 Stem cells derived from cloned human embryos resulting from somatic cell nuclear transfer
6 technology are promising as a potential source of treatment in a wide range of diseases.
7 However, much controversy arises from the necessity to destroy embryos in order to extract
8 their stem cells for use in biomedical research. The conflict centers on the moral status of
9 embryos, a question that divides ethical opinion and that cannot be resolved by medical
10 science.

- 11
- 12 1. While the pluralism of moral visions that underlie this debate must be respected,
13 physicians collectively must continue to be guided by their paramount obligation to the
14 welfare of their patients. In this light, cloning-for-biomedical-research is consistent with
15 medical ethics. An individual physician remains free to decide whether to participate in
16 stem cell research or to use its products.
17
 - 18 2. Cloning-for-biomedical-research requires appropriate oversight and monitoring. At a
19 minimum, not only is the oversight of an institutional review board required, but also that
20 of a regulatory body, such as the Office for Human Research Protections, to monitor
21 progress in the field, assist in developing relevant guidelines, and ensure that the
22 technique of cloning-for-biomedical-research is used only if uniquely promising.
23
 - 24 3. Informed consent by subjects participating in cloning-for-biomedical-research is
25 governed by standard principles: voluntary participation and disclosure of all relevant
26 risks and benefits to subjects. Disclosure to the donor of the oocyte and the donor of the
27 somatic cell also must include:
28
 - 29 (a) description of the procurement procedures specific to the donor;
 - 30 (b) statement of the intention to create a cloned human embryo through introduction of
31 the somatic cell's nucleus into the enucleated egg for research purposes (and not for
32 transfer to a woman's uterus);
 - 33 (c) acknowledgment that the extraction of stem cells will require the cloned embryo's
34 destruction;
 - 35 (d) the intention to derive immortal cell lines from the stem cells to be used in research
36 and possibly in therapeutic contexts; primary and secondary uses should be disclosed
37 and individuals should be free to refuse the use of their biological materials for
38 specified purposes;
 - 39 (e) potential commercial uses and patent or ownership issues (as described in Opinion
40 2.08, "Commercial Use of Human Tissue").
 - 41
 - 42 4. The informed consent process for potential recipients of stem cells derived from cloned
43 embryos should conform with ethical standards outlined in the Council on Ethical and
44 Judicial Affairs' Opinion E-2.07, "Clinical Investigation" and address additional
45 disclosures including provenance of stem cells.

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5. Due to the possibilities of contamination by infectious agents from other species and damage to DNA during growth of new tissues and organs, products of cloning-for-biomedical research raise ethical concerns similar to those surrounding xenotransplantation. Therefore, the informed consent process for potential recipients of these products also should conform to Opinion E-2.169, “The Ethical Implications of Xenotransplantation.”

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CEJA Report 2 – A-99 The Ethics of Human Cloning

INTRODUCTION

In early 1997, a research team in Scotland cloned a sheep, Dolly, by modifying technology developed some decades previously with amphibians. Then, in July of 1998, researchers at the University of Hawaii produced mouse clones and developed a process by which mass cloning could occur. The technique used in both cases, somatic cell nuclear transfer, involves taking a nucleus from a somatic cell, placing it in an enucleated ovum, and implanting the ovum into a host uterus.

The cloning of Dolly brought to the forefront a longstanding debate about cloning human beings. The National Bioethics Advisory Commission recommended a five-year moratorium on any attempts to create a child through somatic cell nuclear transfer in the United States and urged the President to work with all other nations to do the same.ⁱ With the moratorium in place in the United States, legislative attempts to exercise permanent control over human cloning, such as the federal “Prohibition of Cloning of Human Beings Act of 1998,” have been introduced in Congress.

Human cloning is a matter for the medical profession’s attention since it would involve medical procedures and technology, and it may result in the creation of new genetic and psychological conditions that would require professional care. Therefore, the medical profession must evaluate the ethics of human cloning, and in particular, the potential role of physicians in the practice. The Council’s purpose here is to consider whether physicians should participate in human cloning, not to determine whether it should be legal or illegal.

The Council on Ethical and Judicial Affairs offers the following report to assess the ethical uncertainties involved in human cloning. It will address what are currently perceived to be the most widely discussed applications of human cloning, and it will lay the groundwork for future reports. Issues involving embryo research, stem cell research, embryo splitting, embryo twinning, and embryo donor organisms will be addressed in future reports. A scientific analysis of cloning technology can be found in a companion report issued by the Council on Scientific Affairs.

DEFINITIONS

For the purposes of this report, the term “cloning” will refer to the production of genetically identical organisms via somatic cell nuclear transfer.ⁱⁱ “Somatic cell nuclear transfer” refers to the process in which the nucleus of a somatic cell of an existing (or previously existing) organism is transferred into an oocyte from which the nucleus has been removed. “Human cloning” will be used to refer to the application of somatic nuclear transfer technology to the creation of a human being that shares all of its nuclear genes with the person donating the implanted nucleus.

Cloning is distinct from techniques such as embryo splitting and twinning. Human cloning, as defined in this report, does not include the use of somatic cells to create a pluripotent cell line that could, for instance, also be used for extra-uterine production of transplantable tissues without the creation of an entire being. Nor does it include the use of cloning technology for the production of human tissues or human proteins from transgenic mammals.

EXISTING LIMITS ON HUMAN CLONING

Coverage of advances in cloning, especially in the popular press, has described the prospects of manufacturing armies of programmed killers, duplicating sports stars or academic geniuses, and

recreating deceased loved ones.ⁱⁱⁱ Based on the intrinsic limitations of human cloning technology, some widely mentioned undesirable applications of cloning are impossible, and others, which may be possible technically, are clearly prohibited by existing law, public policy, and professional ethical standards. The following sections describe these issues in more detail. In order to clarify the many misconceptions about human cloning, physicians should help educate the public about the intrinsic technical limits of human cloning as well as the ethical and legal protections that should prevent abuses of human cloning.

Replicating specific persons

The term “cloning” may suggest that one organism is the exact replica of another. Human clones would be identical insofar as they would have the same nuclear genes as the donor. However, as observed in natural monozygotic twins, having identical genes does not result in two indistinguishable individuals. A clone must—because of the different environment and circumstances in which he or she creates his or her life story—be a different person from the person from whom he or she was cloned. Although human cloning may be thought of as a sort of “delayed twinning,” twins may be more similar than clones since most twins are conceived and nurtured in the same environment *in utero* and often during childhood. Since environment has a profound influence on development, human clones likely would be different in terms of personality and other characteristics.

Because cloning would not produce exact replicas, several applications of human cloning are illogical. In particular, human cloning would not be a solution to terminal illness or mortality. Children are already thought of as a way to “soften the blow of mortality,” and clones may be seen as a more powerful approach since there is no sharing or mixing of genomes.^{iv} The possibility of having one’s life to live over again, or of getting back a lost child, might be attractive. But the clone would not be the same person as the cloned individual. The fact remains that the person does die and cannot be replaced.

The same reasoning applies to recreating sports stars, dictators, and geniuses—genetics does not wholly define a person. Cloning may allow the persistence of certain genotypes and derived phenotypic traits, but it does not provide individual immortality or replication. A clone of a sports star will not necessarily be a superb athlete, and even if he or she did possess keen athletic ability, he or she would not be identical to the cloned sports star. However, the idea that the clone’s life choices would be affected by other’s expectations raises additional disturbing possibilities that are addressed below.

Creating clones without consent

There is some concern that human clones would be developed from cells obtained without one’s permission since, unlike traditional procreative methods, isolated somatic cells potentially could yield clones. If this technique becomes a possibility, the moral foundations of the therapeutic relationship would have to apply. These include trust, personal respect, and the healer’s fiduciary obligation to serve the patient’s health interests. Any attempt to clone a patient involuntarily would violate all three of these fundamental precepts of medical ethics.

In addition, the doctrine of informed consent would have to apply if this technique becomes a possibility. In Opinion 8.08, “Informed Consent,” the Council has recognized that “the patient should make his or her own determination on treatment.”^v This includes procedures for reproduction. Few exceptions exist to this basic social policy. In addition to ethical safeguards, there are legal protections against procreation without consent. Cloning a patient involuntarily would likely violate the patient’s existing constitutional rights to privacy and reproductive freedom.^{vi} Therefore, under no circumstances should cloning occur without an individual’s permission.

Respecting the rights of clones

Many of the other unrealistic applications of human cloning, such as creating armies of clones or creating human organ factories, stems from the underlying fear that clones would be denied the same rights as other individuals in society. Children are entitled to the same protections as every other individual in society. The fact that a human clone's nuclear genes would derive from a single individual rather than two parents does not change its moral standing. This standard should be applied to every supposed use of clones.

THE REALISTIC USES OF HUMAN CLONING

Assisted Reproduction

There are some realistic applications for cloning technology in the medical arena. One of the most likely uses is as a method of assisted reproduction. To the benefit of many patients, the widespread introduction of assisted reproductive technologies has resulted in a great number of pregnancies and births that otherwise could not have occurred. The use of in-vitro methods of fertilization, donor eggs, donor sperm, and/or surrogate mothers have proved to be effective treatments for infertility. Assisted reproductive technologies are also attractive options to individuals or couples who do not choose to reproduce by traditional means. Cloning technology might allow any couple or individual to reproduce with minimal genetic input from another party.

Because of the prevalence of assisted reproductive technologies and the rapid rate of technological development in this arena, cloning rarely would be the only reproductive option available to prospective parents. For example, scientists recently have pioneered a technique in which DNA is transferred from an infertile woman's oocyte to a viable donor oocyte.^{vii} In addition, the development of somatic cell gene therapy and other technologies may allow for the treatment of genetic disorders—an alternative to avoiding all genetic contribution from a partner with a disease gene. One issue for this report is whether it would be justifiable to make cloning available to individuals who could use existing or alternative options.

Many of the issues that arise in the context of cloning, for example with respect to medical, psychological, or social harms, can be compared to issues that arise in the use of other assisted reproductive techniques. Generally speaking, the medical profession should be satisfied that the benefits of commonly used reproductive interventions outweigh the risks to individuals, families, and their offspring enough to justify medical cooperation with informed patient requests for these services. Evaluating whether or not this calculus has been done for all of the currently used reproductive technologies is beyond the scope of this report. Regardless, cloning should be subject to such a balancing.

In considering cloning as another reproductive health tool, the profession should evaluate whether the ethical concerns introduced by assisted reproductive technologies will be exacerbated in the case of cloning to the point where they outweigh potential benefits to individuals, families, and their offspring. For example, human cloning appears to represent a significant step toward turning children into “products of human will and design,” a situation that many find problematic.^{viii} Determining the balance of possible harms and benefits will require further investigation and discussion regarding human cloning with consideration given to the points raised in the next section.

Individuals do not have a right to demand that physicians participate in human cloning. Before physicians would be justified in participating in human cloning, the harms and benefits need to be evaluated further with some of the issues requiring discussion on a societal level. Until these issues are

brought closer to resolution and benefits clearly outweigh harms, it would be inappropriate for physicians to participate in human cloning.

Tissue Donation

Cloning technology also potentially may be used to create a person with tissues immunologically matched to an existing individual. If the technology uses somatic nuclear transfer for cell or tissue production without creating a human being, then this is not human cloning by the definition used here. One scenario that has been discussed in the context of human cloning is the possibility of manufacturing “donor organisms.” In this context, donor organisms are humans in early stages of development created for the sole purpose of harvesting their organs.^{ix} The creation of human embryo or fetal donor organisms will be addressed in a future report.

Legal and ethical protections already preclude the use of cloned children as discardable donor organisms. Medical ethics is grounded in the principle of nonmaleficence, or the avoidance of harm. Any involvement by a physician in the deliberate sacrifice or harm of children in order to harvest organs would violate this axiom. Further, this practice would be considered murder.

Even where the clone would not be destroyed, the ethical prohibition against using human beings merely as means rather than as ends in themselves makes the possibility of using human cloning to create an organ donor controversial. Nevertheless, even without human cloning, the practice of having children in order to create matching tissue for an older sibling already occurs. One couple unable to find a matching donor for their first child’s bone marrow transplant decided to have a second child on the chance that he or she would also have the rare marrow type.^x Notably, the couple indicated that they had wanted another child and that they would care for the resulting child irrespective of his or her marrow type. In this situation, hoping the child had the same marrow type as its sibling did not preclude the couple from valuing the child for its own sake.^{xi} A cloned person, however, would be born with assurance of tissue compatibility, and perhaps with the expectation of tissue donation.

There are limits on the types of procedures to which parents can consent. In a previous report, “The Use of Minors as Organ and Tissue Donors,” the Council has described the standards that proxies should use when making a decision to donate a minor’s organs.^{xii} One of the standards the Council recommends is a “best interests test” based on the principles of beneficence and nonmaleficence in which the proxy “attempts to ascertain what would bring the most good to the person...and at the very least...do no harm to that person.” Physicians can help parents with the calculus of determining the best interest of the child.

Technological advances in organ and tissue research might alleviate the need to develop a human being in order to produce a matching organ. For example, somatic cell nuclear transfer may be used to produce only the matching, transplantable tissues. Improved pharmaceutical interventions to lower the rate of organ and tissue rejection could also reduce the need for tissue compatibility.

ETHICAL CONCERNS REGARDING HUMAN CLONING

Physicians have an ethical obligation to consider the harms and benefits of new medical procedures and technologies. In weighing the harms and benefits, physicians should consider the possible implications of human cloning. Potential physical harms, psychosocial harms, adverse effects on familial relations, and changes to the gene pool are all legitimate issues. Compared to other technologies that might be used to address reproductive limitations and organ and tissue shortages, these potential harms of human cloning appear to outweigh the potential benefits at this time.

Physical harms introduced by cloning

While the Council will address the harms and benefits of embryo research in a future report, it is important to note that techniques used for cloning humans could potentially endanger the developing individuals. The Human Embryo Research Panel of the National Institutes of Health (NIH), in its 1994 study, advised that embryos should be transferred to a woman's uterus only when "there is reasonable confidence that any child born as a result" will not be harmed.^{xiii} At present, this cannot be assured with any degree of certainty with human cloning. Somatic cell nuclear transfer has not yet been refined and its long-term safety has not yet been proven. The possibility of genetic or cellular conditions, and perhaps an array of illnesses associated with cloning, is of great concern. While the demise of countless amphibian, lamb, and mouse fetuses may be disturbing, similar wastage and mortality among human fetuses is unacceptable. Moreover, we might have significant concerns about offering such technology to women as a mechanism to facilitate reproduction given the potential harms from the expected high miscarriage rate.

The risk of producing individuals with developmental anomalies is serious and precludes human cloning for the time being. Producing disabled human clones would give rise to an obligation to seek better understanding of—and potential medical therapies for—the unforeseen consequences that could arise from human cloning.

Psychosocial harms introduced by cloning

Human cloning has the potential to introduce psychosocial harms to individuals. If a person with known genetic predispositions and conditions is cloned, the cloned child's genetic predispositions and conditions will, due to the very nature of cloning, also be known to a certain extent. For the most part, environment will also play a significant role. Presently, a child's genetic predispositions can be predicted to varying degrees if the parent's genetic predispositions have been determined. Knowledge of a child's genetic predispositions raises concerns about the autonomy and best interests of the child. The Council has urged caution in this area in its ethical Opinion 2.138, "Genetic Testing of Children."^{xiv} Knowledge of genetic information holds great significance to an individual. The harm of preempting the child's future choice in knowing or forgoing knowledge of his genetic status and the danger of abrogating the child's right to privacy with respect to this status must be weighed carefully.

Foregoing choice in learning one's genetic predispositions may seem trivial compared to the concerns about identity raised with human cloning. If raised by the clone-parent, a clone-child could see what he or she has the potential to become. In this respect, human clones would differ dramatically from monozygotic twins who develop simultaneously. The timing of development is a key difference between monozygotic twins and human clones. Having insight into one's potential may cause enormous pressures to live up to expectations (or inappropriately relieve pressure to do so), even more so than those generally experienced by children.

Presumably, a person would clone him or herself or another individual because that person has desirable characteristics that would be reflected in the clone. For example, the person who cloned a sports star presumably would hope that the clone-child develops into another sports star. A sports star's clone-child unable to live up to these expectations could be dubbed a failure unable to capitalize on his or her genetic gift. Moreover, although the clone-child of a sports star might feel more confident of his or her abilities from the outset, other clone-children may feel limited by their genetic lot. If a clone-child saw that he or she was likely to develop certain diseases or had failed at certain tasks, his or her undertakings might be bounded by what the clone-parent had done. Therefore, cloning might limit the clone-child's perception of self and increase external pressures. Human cloning may diminish, at least psychologically, the seemingly unlimited potential of new human beings and may exacerbate disturbing motivations for having children.

The impact of human cloning on family and society

In addition to concerns about individual privacy and identity, the implications of cloning for family and broader social relationships remain uncharted. What would be the consequence to, say, the father-daughter relationship if the daughter and wife were genetically identical? Would a woman have a normal mother-daughter relationship with her clone?^{xv} These examples illustrate that the family unit might be quite different with the introduction of cloning. As one philosopher wrote: “cloning shows itself to be a major violation of our given nature as embodied, gendered, and engendering beings—and of the social relations built on this natural ground.”^{xvi}

Additionally, some problems are technical and legal in nature. For instance, birth cousins could be genetic siblings, and this might result in a need to revisit laws governing marital eligibility. Also, the courts have had difficulty sorting out parental rights in cases of assisted reproduction. In one case, a court found a child conceived using assisted reproductive technologies to have no parents despite having eight individuals from which to choose.^{xvii}

While discussion and resolution of these issues is not the province of physicians, the impact of human cloning on family and society is an important factor for physicians to consider when weighing the costs and benefits of cloning. Until more thought is given on a societal level regarding how to construct familial relations in this context, physicians should not participate in human cloning.

The effects of human cloning on the gene pool

Although not the most imminent threat, human cloning has the potential to alter the gene pool. In order for human cloning to have a significant effect on the gene pool, cloning would have to be widespread, and clones would have to reproduce. If cloning became widespread, human genetic diversity would decrease. Over time, the benefits of genetic diversity, from having individuals with disease immunity to fostering a population with a wide variety of talents, have helped human beings survive and succeed.

Like other interventions that can change individuals’ reproductive patterns and the resulting genetic characteristics of a population, human cloning raises the specter of eugenics.^{xviii} The possibility that physicians might play a part in deciding which persons are or are not “worthy” of cloning is contrary to professional medical values by all respectable accounts. For the most part, those individuals thought to possess desirable characteristics or lack undesirable ones would be cloned. In addition, as is the worry with many assisted reproductive technologies, only those who have the ability to pay or are members of favored social groups will have access. This would have the potential to skew the gene pool in the direction of favored social groups and whatever characteristics are thought to be advantageous at the time, even though the long-term desirability of the characteristics is unknown.^{xix} The possibility that physicians might be the agents of a social policy that make such judgments is contrary to professional medical values.^{xx} The application of cloning for eugenic or discriminatory practices is incompatible with the ethical norms of medical practice.

In addition, since the somatic cell from which clones originate likely will have acquired mutations, serial cloning would compound the accumulation of mutations that occur in somatic cells. Although these mutations might not be apparent at the time of cloning, genetic problems could become exacerbated in future generations. These possibilities need to be investigated further before physicians participate in human cloning.

THE NEED FOR INTERNATIONAL REGULATIONS

Even if the United States developed sound ethical guidelines and well-crafted regulations to address the practice of human cloning, some fear that human cloning would simply be forced into other locales. Individuals could travel to other countries where human cloning would be available and potentially unregulated. Because cloning technology is not limited to the United States, physicians should help establish international guidelines regarding human cloning.

CONCLUSION

Human cloning raises a variety of concerns, some realistic and others less so. It would be irresponsible to forge ahead with this new technology in the absence of serious discussion regarding the possible harms and benefits of cloning human beings. Until the benefits of human cloning are thought by society to outweigh the harms, it would be inappropriate for physicians to participate in human cloning.

RECOMMENDATIONS

The Council on Ethical and Judicial Affairs recommends that the following be adopted and that the remainder of this report be filed:

For the purpose of these guidelines, “somatic cell nuclear transfer” refers to the process in which the nucleus of a somatic cell of an organism is transferred into an oocyte from which the nucleus has been removed. “Human cloning” refers to the application of somatic nuclear transfer technology to the creation of a human being that shares all of its nuclear genes with the person donating the implanted nucleus. Human cloning, as defined in this report, does not include the use of somatic cells to create a pluripotent cell line that could, for instance, also be used for extra-uterine production of transplantable tissues without the creation of an entire being. Nor does it include the use of cloning technology for the production of human tissues or human proteins from transgenic mammals. This report does not address the issue of embryo or cloning research, stem cell research, embryo twinning, or embryo splitting.

- 1) In order to clarify the many existing misconceptions about human cloning, physicians should help educate the public about the intrinsic limits of human cloning as well as the current ethical and legal protections that would prevent abuses of human cloning. These include the following:
 - a) using human cloning as an approach to terminal illness or mortality is a concept based on the mistaken notion that one’s genotype largely determines one’s individuality. A clone-child created via human cloning would not be identical to his or her clone-parent.
 - a) current ethical and legal standards hold that under no circumstances should human cloning occur without an individual's permission.
 - a) current ethical and legal standards hold that a human clone would be entitled to the same rights, freedoms, and protections as every other individual in society. The fact that a human clone’s nuclear genes would derive from a single individual rather than two parents would not change his or her moral standing.
- 1) Physicians have an ethical obligation to consider the harms and benefits of new medical procedures and technologies. Physicians should not participate in human cloning at this time because further investigation and discussion regarding the harms and benefits of human cloning is required. Concerns include:

- a) unknown physical harms introduced by cloning. Somatic cell nuclear transfer has not yet been refined and its long-term safety has not yet been proven. The risk of producing individuals with genetic anomalies gives rise to an obligation to seek better understanding of—and potential medical therapies for—the unforeseen genetic consequences that could stem from human cloning.
 - b) psychosocial harms introduced by cloning, including violations of privacy and autonomy. Human cloning promises to limit, at least psychologically, the seemingly unlimited potential of new human beings and to create enormous pressures on the clone-child to live up to expectations based on the life of the clone-parent.
 - c) the impact of human cloning on familial and societal relations. The family unit would be different with the introduction of cloning, and more thought is required on a societal level regarding how to construct familial relations.
 - d) potential effects on the gene pool. Like other interventions that can change individuals' reproductive patterns and the resulting genetic characteristics of a population, human cloning has the potential to be used in a eugenic or discriminatory fashion—practices that are incompatible with the ethical norms of medical practice. Moreover, human cloning could alter irreversibly the gene pool and exacerbate genetic problems that arise from deleterious genetic mutations, resulting in harms to future generations.
- 2) Two potentially realistic and possibly appropriate medical uses of human cloning are for assisting individuals or couples to reproduce and for the generation of tissues when the donor is not harmed or sacrificed. Given the unresolved issues regarding cloning identified above, the medical profession should forsake human cloning at this time and pursue alternative approaches that raise fewer ethical concerns.
 - 3) Because cloning technology is not limited to the United States, physicians should help establish international guidelines governing human cloning.

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