

## STEM CELL RESEARCH AND CLONING—SCIENCE AND ETHICS (revised)

Sharon Quick, MD, FCP, FAAP  
Washington State Coordinator, American Academy of Medical Ethics

### DEFINITIONS

Stem cells: Cells that have the capacity to produce more cells of the same or other tissue types. They can continue dividing for an indefinite period of time; other cells cannot do this. Two sources of stem cells are embryonic stem cells and adult stem cells. Embryonic stem cells can be obtained from sexually-produced embryos such as those left over from in vitro fertilization (IVF) or from cloned embryos.

Embryo: A one-celled embryo is first formed with the union of an egg and a sperm. This cell divides and grows, implanting in the uterus when it has grown into a hollow ball of cells at approximately 1 week of age in humans. At 8 weeks of age the human embryo is called a fetus; there is not a significant change in any developmental characteristics at this time—it is simply a name change. NOTE: There is no such entity as a “pre-embryo.” A “pre-implantation embryo” refers to an embryo before its implantation in the uterus.

Embryonic stem cells (ESCs): Cells derived from an embryo at about 1 week of age. The embryo is killed in the process of obtaining these cells. The cells are then grown in the lab. Embryonic stem cells are difficult to establish and maintain in culture. Many human embryos are sacrificed to obtain a few stem cell lines. For example, in the spring of 2004, a Harvard group used 342 human embryos to obtain 17 stem cell lines.<sup>1</sup> Researchers attempt to induce these cells to turn into different kinds of tissue by exposing them to different growing conditions.

Embryonic stem cell line: Embryonic stem cells growing in the lab that are derived from 1 embryo that has a unique genetic code representing a unique human individual. These human embryonic stem cell lines can be patented.

Adult stem cells (ASCs): Stem cells derived not only from adults, but from children, infants, placenta, and umbilical cord blood. ASCs are found in many different tissue types: bone marrow, fat, pancreas, heart, brain, intestines, etc. There is also evidence that ASCs of one tissue type can be induced to form a different tissue type (pluripotential). ASCs can proliferate in culture.<sup>2-5</sup>

Cloning (aka somatic cell nuclear transplantation): Combining the following 2 cells to form a 1-celled embryo: (1) a body cell of one animal and (2) an egg cell that has had its nucleus containing the chromosomal DNA removed. Once this one-celled cloned embryo has been formed, the process of cloning is complete. This cloned embryo is nearly the genetic twin of the animal from which the body cell was taken. The cloned embryo is induced to divide and grow until it reaches a hollow ball stage at which point it has 2 possible fates:

1. Implantation into a uterus with the purpose of a live birth—so-called “reproductive cloning”
2. Destruction to obtain its embryonic stem cells—so-called “therapeutic cloning.”

In vitro fertilization (IVF): Uniting eggs and sperm outside a woman's body in a lab. When an egg is "fertilized" by union with a sperm, an embryo is formed.

HUMAN EMBRYONIC STEM CELL RESEARCH and HUMAN CLONING ARE UNSAFE, UNNECESSARY, AND UNETHICAL. THIS RESEARCH DESTROYS HUMAN EMBRYOS, MAY HARM PATIENTS, AND WILL EXPLOIT WOMEN.

### **UNSAFE**

It is hard to control the differentiation (what the cells turn into) of embryonic stem cells (ESCs); they have a tendency toward tumor formation.<sup>6-9</sup> Recipients of ESC products would likely require anti-rejection medications. ESC lines that are maintained for longer periods of time have been shown to have genetic defects, making them unsuitable for use in humans.<sup>10</sup> There are no human trials with ESCs, and animal studies have had few successes and many complications. It would be unsafe and a profound breach of scientific ethics to proceed with human trials with ESCs when their use in animals has not been widely successful.

### **Cloning:**

When ESCs are derived from cloned embryos there are further problems.

**Harm to embryo**--Destruction of a human cloned embryo or fetus to obtain stem cells or tissue destroys a human life. Many embryos are killed in the derivation of one stem cell line.

### **Harmful to patients**

- Clones are defective. Not all genes are activated in cloned embryos as they are in noncloned ones. The majority of cloned embryos cannot even proceed with cell division, and those that are able to do so have multiple abnormalities: genetic abnormalities, premature aging, large offspring syndrome, etc.<sup>11-14</sup> Dolly the cloned sheep died at age 6, when a normal sheep's lifespan is 11-12 years, and she was plagued by arthritis and lung problems. Such predisposition to disease and abnormalities is present in the original cloned embryo; thus anyone receiving cloned products derived from embryos or fetuses will be receiving diseased tissue. Current standards of organ transplantation prevent the use of diseased organs or tissue; cloned products should fall into this category.
- Cloned cells or tissue may be rejected by the patient into whom such products are implanted. Experts have stated that patients receiving cloned products will likely need to take anti-rejection medications. {NOTE: Dr. John Gerhart, transcript of the April 25, 2002 meeting of the President's Council of Bioethics; p. 47; }<http://www.bioethics.gov/meetings/200204/0425.doc> } {NOTE: Dr. Irving Weissman, Stanford, before the President's Council on Bioethics on Feb. 13, 2002} The explanation for this fact is beyond the scope of this letter.
- Cloning has not been successful in curing animals of disease—it would be unconscionable to progress to human cloning for research purposes

### **Harmful to women**

- Human cloning is very inefficient. According to a report in Science, 16 women donated a total of 242 eggs for the only published human cloning experiment. 30 cloned embryos reached the blastocyst stage where embryonic stem cells can be obtained. Only one embryonic stem cell line was established. To date, no therapies or treatments exist that use such cells." (<http://www.cbhd.org/media/pr/2004-02-12.htm>)

- Because of the inefficiency of the cloning process, its use in humans will subject a large population of women to health risks intrinsic to harvesting the enormous quantities of eggs required. Such risks include complications from medications to increase egg production, surgical risks, and a possible increase in the probability of ovarian cancer. It is estimated that the use of cloning to treat just one patient group, the 17 million diabetics in the U.S., will require approximately 85 million women to “donate” eggs. Such egg harvesting is impractical since there are only 60 million women of childbearing age in the U.S. Do the math—this would create a shortfall of about 25 million--Human eggs may become a commodity, with exploitation of disadvantaged women around the world.<sup>18</sup>
- There are pro-life and pro-choice women coming together to oppose all forms of human cloning.

### **Unsuccessful**

- There are no human studies showing therapeutic applications.
- Cloning studies in animals have been largely unsuccessful except if the cloned animal is brought to fetal stages or through birth, and has fetal tissues or adult stem cells harvested for transplant back into the original diseased animals.<sup>19, 20</sup> Even then, the positive results are sparse, and long-term effects have not been established. It would be unsafe to proceed with human trials.

### **UNNECESSARY**

Adult stem cells (term includes stem cells from adults, children, infants, placenta, and umbilical cord blood) are already accomplishing what ESC research only hopes to do.

Adult stem cells (ASCs) are safe:

1. Avoid the problems with tumor formation seen with ES cells.
2. Can be obtained from the individual that will later receive cells so there is no transplant rejection.
3. No risk of transferring genetic, viral or other disease vectors when cells come from the same person.

ASCs are ethical as they do not require the destruction of human life.

While embryonic stem cells have not been used in one human trial, ASCs are currently being used successfully in human trials for a variety of diseases.

### **Some Current Clinical Uses of Adult Stem Cells in Humans**

- Cancers—Lymphomas, multiple myeloma, leukemias, breast cancer, neuroblastoma, renal cell carcinoma, ovarian cancer
- Autoimmune diseases—multiple sclerosis, systemic lupus, rheumatoid arthritis, scleroderma, scleromyxedema, Crohn’s disease
- Anemias (incl. sickle cell anemia)
- Immunodeficiencies—including human gene therapy
- Bone/cartilage deformities—children with osteogenesis imperfecta
- Corneal scarring-generation of new corneas to restore sight
- Stroke—neural cell implants in clinical trials
- Repairing cardiac tissue after heart attack—bone marrow or muscle stem cells from patient
- Parkinson’s—retinal stem cells, patient’s own neural stem cells, injected growth factors
- Growth of new blood vessels—e.g., preventing gangrene

- Gastrointestinal epithelia—regenerate damaged ulcerous tissue
- Skin—grafts grown from hair follicle stem cells, after plucking a few hairs from patient
- Wound healing—bone marrow stem cells stimulated skin healing

Example of adult stem cell research working better than that with ESCs in animals: 2 experiments with diabetic mice, one using ESCs, the other ASCs

1. ESC experiment: ESCs obtained from mice and stimulated to form insulin-producing cells. These cells were transplanted into diabetic mice; unfortunately, not enough insulin was produced and the mice died<sup>21</sup>
2. ASC experiment: Pancreatic stem cells obtained from adult mice and form insulin-producing cells. These cells are transplanted into the diabetic mouse; 100% of the needed insulin is produced and the mouse is cured<sup>22</sup>

### **Economics**

Concern has been expressed that Washington State may lose biotechnology companies or researchers to other countries if we don't enact legislation approving embryonic stem cell research. First of all, there is no ban on embryonic stem cell research at either the federal or Washington State level. The only ban is on federal funding of research in which human embryos are destroyed. In fact, President Bush lifted this ban to allow funding of certain ESC lines that had already been produced. Secondly, there is no evidence that states that ban human embryo research do poorly in the biotechnology arena. In fact, states that have passed BANS on human cloning and/or embryonic stem cell research are rapidly growing in the biotechnology industry.

Example: Pennsylvania also has a longstanding ban on harmful experiments on human embryos; such experimentation is a Class C felony. Under this policy, Pennsylvania now "ranks second in pharmaceutical employment nationally, third in biotechnology employment and fourth in medical device employment" in the United States ([www.pabioconnect.com/aboutbio.html](http://www.pabioconnect.com/aboutbio.html)). [Information from <http://www.usccb.org/prolife/issues/bioethic/embryo/growth1404.htm> ]

### **UNETHICAL**

#### **Human life begins with the 1-celled embryo**

ESC research using cloned or noncloned embryos requires killing human lives to obtain these cells. When does a human life begin?

Biology and embryology textbooks state that human life begins with the 1-celled embryo, or zygote, which is formed with the union of an egg and a sperm:

- "A zygote is the beginning of a new human being."<sup>23</sup>
- "Life began for each of us with the fusion of...a sperm and an ovum."<sup>24</sup>

Cell biology has defined living organisms as carrying out various "life functions" such as Nutrition, Transport, Respiration, Synthesis, Assimilation, Growth, Excretion, Regulation, Reproduction, and Metabolism. All life from the simplest one-celled amoeba to complex animals carry out these life functions in various ways. Human embryos carry out the

same life functions as humans at later developmental stages, only they may do so differently. One cannot classify a human embryo as “not living” without also refuting basic principles of cell biology.

### **Human personhood**

There are some who would admit that a human embryo is living, but deny that it has full personhood. However, there is no standard on the continuum of life (beginning with a 1-celled embryo and continuing through birth and adulthood to the point of death) by which an individual on this journey can be classified as “not human,” without the risk of compromising the rights of humans at a later stage of development.

Examples of “personhood” standards that are not viable:

1. An embryo is not worthy of human rights until it is implanted in a uterus---Implantation is merely a change of location for a living embryo; personhood should not be based on factors extrinsic to the human. Many embryos conceived within a woman die a natural death because they do not implant, but that is very different than actively killing them.
2. Embryos and fetuses don't have rights because it is just like abortion---The legal basis for permitting abortion was not a lack of embryo/fetal rights, but purported competing Constitutional rights of women and their unborn children. In the case of embryo research, there are not competing rights, and an embryo's right to life should not be sacrificed for the purported benefit of medical research. Unlike abortion, there is no conflict between a woman's right over her own body and the right of an embryo to life. Pro-choice people can still hold their position while opposing this research.
3. An embryo lacks brain activity or nervous system functioning---The life function of coordination (regulation), involving communication and control of activities within the organism and its interaction with the environment, is carried out without any specialized system in the early embryo. Beyond 2 weeks of life, the nervous system, in part, carries out this function. Throughout life, human growth and development, as well as disease states, involve changes in the way life functions are performed. One would not expect an infant to speak in words, walk, or function independently given the child's immature nervous system. Yet, that does not mean a baby does not have intrinsic human worth and full rights. Embryos carry out life functions in a developmentally appropriate way that is different than a human at a later stage of development; classifying them as having less than full human rights is discriminatory.

Throughout history, people have been discriminated against because of race, religion, nationality, etc. Less than 200 years ago in our country, a group of people were assessed to be 3/5 a person based on skin color. Sometimes people have been subject to unethical research with “the end justifies the means” mentality. Children who were “just going to die anyway” were placed under forced experimentation in Nazi concentration camps. Black syphilis patients went for years without treatment in the US so that the effects of the disease could be studied.

Worldwide medical codes such as the Nuremburg Code, developed after medical research atrocities in German concentration camps, prohibit research without the consent of the research subject, and prohibit research in which death or disabling injury occur. The embryo cannot give consent for ESC research, and is killed for the presumptuous benefit of another.

Today there is another group of humans that needs governmental protection from discrimination—embryos. Is the fact that embryos carry out their life functions in a developmentally appropriate way that is different than a human at a later stage of development a reason to classify them as having less than full personhood? If it is, then infants and children are also not fully persons. Most people admit that a human embryo deserves some measure of respect, if not full entitlement to personhood. Even in IVF clinics, embryos are sometimes given funerals prior to being killed. How much of a person is an embryo? When does a human achieve full personhood? Are rights in proportion to how much of a person one is declared to be? What protection should be granted to a human who is assessed to be half a person? Would he or she receive half a share of the right to life? How would that be accomplished?

### **Impracticality of Destructive Human Embryo Research—and possible exploitation of women**

If ESC research is to be widely used, it is doubtful that it would be limited to “leftover” embryos.

A 2002 RAND Corporation survey of IVF clinics in the United States (found at [www.stemcellresearch.org](http://www.stemcellresearch.org)) finds:

- The vast majority of the 400,000 currently frozen embryos — 88.2% — are being held for family building, NOT slated for destruction.
- 2.2% are slated to be discarded.
- 2.8% (about 11,000) have been designated to be destroyed for their stem cells for research purposes.
- Only a small number of those 11,000 embryos would actual yield stem cells. Using what it calls “a conservative estimate” the RAND study calculated that only about 275 stem cell lines could actually be developed from the embryos available for research. And even then, the RAND study concedes that this number “is probably an overestimate.

If human embryo freezing techniques become better and/or efficiency of producing stem cell lines improves, it is possible that there could be an increase in the number of ESC lines produced from a given number of frozen embryos.

However, the advancing technology of egg freezing may obviate freezing human embryos at all in the future. There are centers now offering human egg freezing on an investigational basis, and a handful of children have been born, each of whom started life from a frozen egg. Egg freezing, for example, is currently being offered as an investigational procedure at the Fertility Institute in Los Angeles. ([http://www.fertility-docs.com/news\\_events.phtml](http://www.fertility-docs.com/news_events.phtml))

Given the inefficiency of producing ESC lines and the lack of sufficient numbers of frozen embryos, it is probable that biological factories would have to be developed that create human embryos for the sole purpose of performing destructive research on them. Again, we are back to exploiting women who would have to donate eggs to make such research a reality. Some researchers have proposed an alternative to using women’s eggs by using ESCs to make germ cells (eggs and sperm) to make more embryos to make more ESCs. Biological factories are exactly what would need to happen in order for “therapeutic” cloning to become a reality, as well.

### **Destructive human embryo research ultimately harms the diseased and disabled**

Society must answer the question: what price are we willing to pay to end disability? Laws and medical ethical codes have established a boundary that has preserved human life as intrinsically valuable. If that line is crossed by sacrificing human embryos in the name of medical progress, a step has been taken down that slippery slope of redefining the value of human life so that it is no longer intrinsic, but conditional. The qualifications for personhood can be changed by whoever has the power to do so; anyone whose defects don't meet the standards for personhood loses their rights. The very people that human ESC research aims to help--those who fall into the category of "diseased" or "disabled"-- will be vulnerable to that slippery slope of being classified as "undesirables" whose lives are deemed to be "not worth living" and can be sacrificed in the name of medical progress. The many disabled children and their families that I have cared for over the years have not seen their lives as "not worth living." The diseased and disabled are a blessing, not a burden. Certainly society should aim to eliminate disease, but not by eliminating people. Destroying human life in the name of science will ultimately corrode science.

### **Some issues for speculation and further investigation:**

Given that:

- There is no law against human ESC research, yet small numbers of private investors in this research.
- There are no human ESC research clinical trials in humans, and very minimal successes and many failures in animal ESC research
- Human ESC lines can be patented.

Then.....Is the push for government via taxpayer dollars to fund human ESC research an attempt to see if it's successful before investors risk capital? Is the lure of profits from patented human embryonic stem cell lines a driving force that presents a bias in evaluating the science and ethics?

### **CONCLUSION**

We can be remembered as a society that cares for their children, promoting life and liberty for all Americans, regardless of age and size and developmental stage. Or we can be remembered as a society that allowed another holocaust. The scientific data support adult stem cell research as being the best investment for our research dollars with the most likely chance of producing new, safe, and ethical cures in the lifetimes of those patients who are living now. If Washington State invests its limited research dollars into adult stem cell research, it will be a leader in making the hope for a cure a reality, instead of wasting dollars on unsafe, unethical, and unnecessary research with human cloning and human embryonic stem cells.

### References

1. Prentice DA. Testimony of Dr. David Prentice. *Embryonic Stem Cell Research: Exploring the Controversy*. Washington D.C.: U.S. Senate Committee on Commerce, Science, and Transportation; 2004.

2. Colter DC, Class R, DiGirolamo CM, Prockop DJ. Rapid expansion of recycling stem cells in cultures of plastic-adherent cells from human bone marrow. *Proc Natl Acad Sci U S A*. 2000 Mar 28;97(7):3213-3218.
3. Jiang Y, Jahagirdar BN, Reinhardt RL, et al. Pluripotency of mesenchymal stem cells derived from adult marrow. *Nature*. 2002 Jul 4;418(6893):41-49.
4. Krause DS. Multipotent human cells expand indefinitely. *Blood*. 2001 November 1;98(9):2595.
5. Reyes M, Lund T, Lenvik T, Aguiar D, Koodie L, Verfaillie CM. Purification and ex vivo expansion of postnatal human marrow mesodermal progenitor cells. *Blood*. 2001 Nov 1;98(9):2615-2625.
6. Vogel G. Can Adult Stem Cells Suffice? *Science*. 2001 June 8;292:1820-1822.
7. Schuldiner M, al. e. Effects of eight growth factors on the differentiation of cells derived from human embryonic stem cells. *Proc. Natl. Acad. Sci. USA*. 2000 Oct. 10;97:11307-11312.
8. Odorico JS, Kaufman DS, Thomson JA. Multilineage differentiation from human embryonic stem cell lines. *Stem Cells*. 2001 19:193-204.
9. Lanza RP, Cibelli JB, West MD. Human therapeutic cloning. *Nature Medicine*. 1999 September;5:975-977.
10. Clayton J. Human stem cells show abnormalities. *BioMedNet-Molecular Medicine Gateway*. Available at: <http://gateways.bmn.com/molecular-medicine/news?uid=NEWS.031224-1>. Accessed Feb. 7, 2004.
11. Allen J, Allen C. A mitochondrial model for premature aging of somatically cloned mammals. *IUBMB. Life*. 1999 Oct.;48(4):369-372.
12. Humpherys D, al. e. Epigenetic instability in ES cells and cloned mice. *Science*. 2001 July 6;293:95-97.
13. Vastag B. Epigenetics seen as possible key to cloning. *JAMA*. 2001 Sept. 26;286(12).
14. Vastag B. At the cloning circus sideshows abound, while scientist seek a wider audience. *JAMA*. 2001 Sept. 26;286(12).
15. Dr. John Gerhart, transcript of the April 25, 2002 meeting of the President's Council of Bioethics; p. 47; (<http://www.bioethics.gov/meetings/200204/0425.doc>)
16. Dr. Irving Weissman, Stanford, before the President's Council on Bioethics on Feb. 13, 2002
17. Personal communication with David Prentice, PhD, cell biologist and professor at Indiana University
18. Do No Harm. Do the Math: Experimental Cloning Exploits Women. Available at: <http://www.stemcellresearch.org/info/dothemath.htm>. Accessed March 1, 2003.
19. Rideout WM, al. e. Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy. *Cell*. 2002 April 5;109:17-27.
20. Lanza R, al. e. Generation of histocompatible tissue using nuclear transplantation. *Nature Biotechnology*. 2002 July;20:689-696.
21. Lumelsky N, Blondel O, Laeng P, Velasco I, Ravin R, McKay R. Differentiation of embryonic stem cells to insulin-secreting structures similar to pancreatic islets. *Science*. 2001 May 18;292(5520):1389-1394.

22. Ramiya VK, Maraist M, Arfors KE, Schatz DA, Peck AB, Cornelius JG. Reversal of insulin-dependent diabetes using islets generated in vitro from pancreatic stem cells. *Nat Med.* 2000 Mar;6(3):278-282.
23. Moore K. *The Developing Human: Clinically Oriented Embryology*. 4th ed. Philadelphia, PA: W.B. Saunders Company; 1988.
24. Curtis H. *Invitation to Biology*. Second ed. New York, NY: Worth Publishers; 1977.