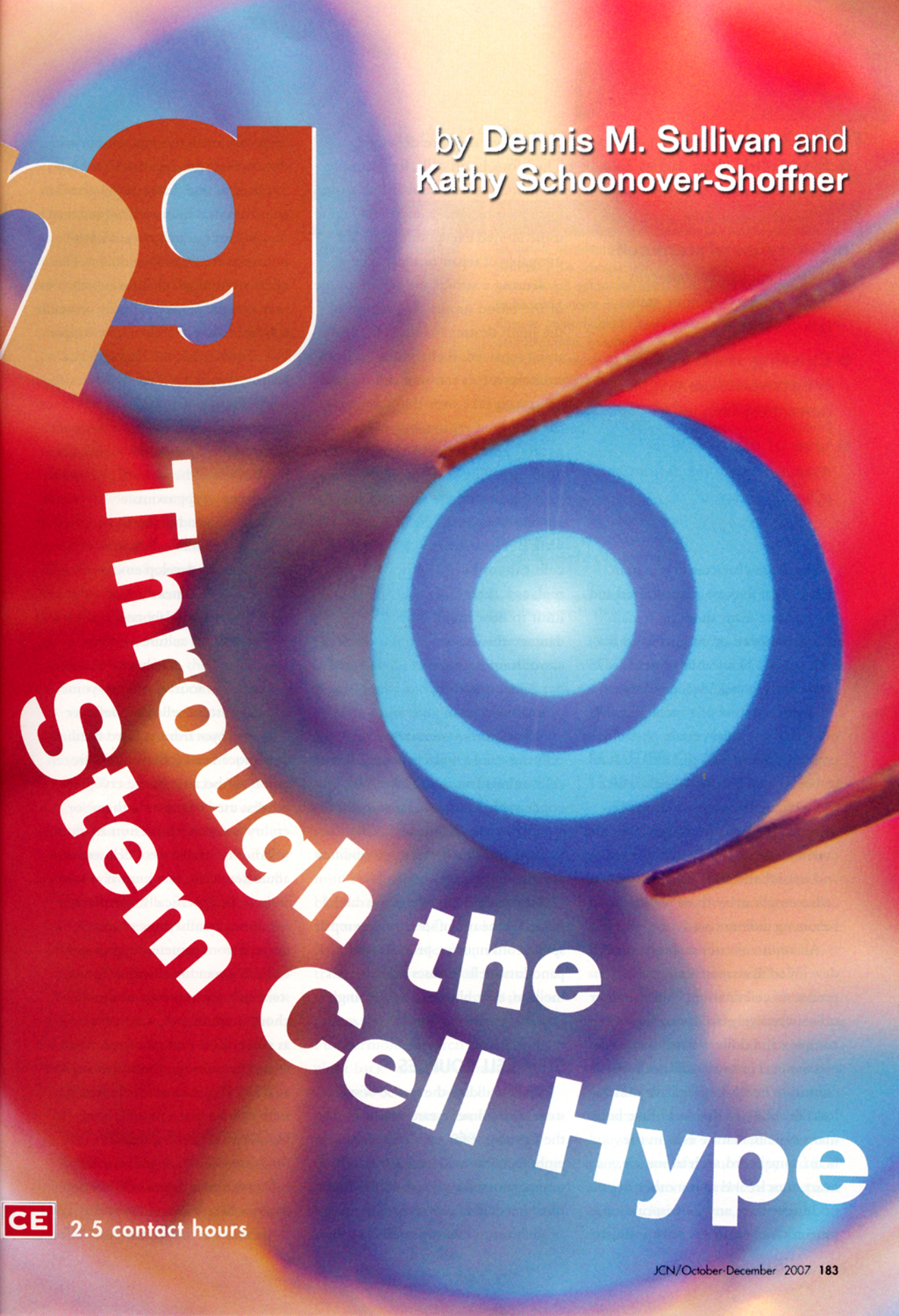

Through the Stem Cell Hype

by Dennis M. Sullivan and Kathy Schoonover-Shoffner

CE 2.5 contact hours

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As Nancy cared for her patient who had received a somatic stem cell transplant to repair heart muscle damage to the left ventricle, she marveled at this new treatment for those suffering severe muscle damage and cardiac insufficiency after myocardial infarction. The transplant unit had become quite busy caring for patients undergoing stem cell transplantation procedures, as new cures for common diseases and trauma were made available. She wondered what malady stem cell transplants would cure next.

Sound far fetched? On the basis of current biotech research, such stem cell transplantations may not be too far off in the future. We read about tantalizing research aimed at changing our genetic makeup and lengthening human life. We hear from famous people such as the wife of former president Ronald Reagan, Michael J. Fox, and baseball standout Ron Santo about what stem cell transplants can do for those with Alzheimer's dementia, spinal chord injury, Parkinson's disease, diabetes, and arthritis.

Nigel Cameron (2005), research professor of bioethics, has called this the "biotech century," which certainly is apt given all of the excitement over new ways to intervene in biology and medicine. At the forefront of all the new biotechnologies is the "holy grail" of embryonic stem cell research, attracting a lot of media attention and investment money.

Are stem cell transplants a panacea for what ails us? And what exactly is involved in stem cell transplants? What, to date, tangible returns have occurred from stem cell research? To answer such questions for our clients, friends, and ourselves, nurses need a basic understanding of stem cells, current research, and the ethical debate surrounding embryonic stem cells.

Dennis M. Sullivan, MD, is professor of Biology at Cedarville University, Cedarville, Ohio, where he teaches human biology and bioethics. He is Director of the Center for Bioethics at Cedarville University, the author of numerous articles in *Ethics and Medicine* and other journals, especially in the area of human personhood. He and his wife Barbara live in Beavercreek, Ohio.

Kathy Schoonover-Shoffner, PhD, RN, serves as editor of *JCN* and as a staff worker with Nurses Christian Fellowship. She works per-diem as a staff nurse with Via Christi Behavioral Health in Wichita, KS. Kathy is married, has three teenagers, and attends First Baptist Church in Wichita.

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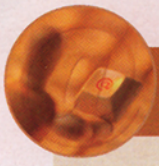
WHAT ARE STEM CELLS?

Human stem cells are the "starter" cells that act as precursors of mature bodily tissues. Such cells have not yet differentiated (become specialized) into their mature forms. All human beings possess such cells. For example, precursors of mature blood cells are the pluripotent stem cells of the bone marrow. Such cells are called "pluripotent" (from Latin roots for "many" + "powers") because one of these undifferentiated cells can become any of a variety of different blood cells. These include the various white blood cells that protect against bodily infection, the platelets that help the blood to clot, and the red blood cells that carry oxygen throughout the body.



at a Glance

- **Stem cell therapies** *hold promise for treating a wide range of disease, tissue damage, or both.*
- **Two types of stem cells exist:** *embryonic stem cells (hES) and adult somatic stem cells (ASSC).*
- **Existing stem cell treatments** *use ASSC; no current treatments use hES.*
- **Use of hES cells** *for research requires the destruction of human embryos.*

Important characteristics of stem cells are that they are unspecialized and can replicate many times yet remain undifferentiated or unspecialized for long periods. This feature of stem cells allows for "cloning," or the generation of identical copies of a molecule, cell, or organism. Under certain physiologic conditions stem cells can be induced to become differentiated cells with special functions such as the insulin-producing cells of the pancreas. Scientists continue to study the conditions within and outside the cell that allow stem cells to replicate with or without becoming differentiated.

All adult cells in our body once developed from stem cells by the process of cell division, with daughter cells successively becoming more complex and differentiated than their precursors. However, adult cells that constitute bodily organs have mostly lost the ability to divide. Unlike bone marrow cells, mature cells in the brain, spinal cord, skeletal muscle, heart muscle, and many other organs no longer have any corresponding pluripotent stem cells to repopulate them when they are damaged. Therefore, brain cells, for example, are limited to the number that arose from their original stem cells. Despite some limited exceptions, these are incapable of repair or replacement.

During a stroke, sudden blockage of the blood supply to a region of the brain destroys brain cells, never to be replaced. Rehabilitation from a stroke involves training other brain centers to take over the function of the damaged region, but there is no natural process that can replace the dead cells. The same problem occurs in the heart, where repeated heart attacks weaken the heart wall. Because heart cells cannot be replaced, there is a limit to how much damage the heart can sustain before permanent disability or death occurs.

To date, no embryonic stem cell treatments have been successful in laboratory or clinical models.

What if there were stem cells that could replace damaged brain cells or heart muscle? This could conceivably improve a person's life span or at least the quality of the person's life. The biologic possibilities are intriguing.

An equally compelling case can be made for the use of stem cells to repair spinal cord injuries, provide new pancreatic cells in cases of diabetes mellitus, treat blindness or hearing loss, or cure Parkinson's disease.

STEM CELL SOURCES

What could be the source of such stem cells? Some researchers claim that the best source for stem cells is a human embryo, composed exclusively of unprogrammed early stem cells, any one of which could become the precursor of adult tissues and organs. Embryonic stem cells are derived from embryos developing from eggs that have been fertilized *in vitro* (Latin for "in glass") in an in vitro fertilization clinic and then donated for research purposes with informed consent of the donors. The embryos from which human embryonic stem cells are derived typically constitute a 4- or 5-day-old hollow microscopic ball of cells called the *blastocyst*. The blastocyst includes three structures: the *trophoblast*, which is the layer of cells that surrounds the blastocyst; the *blastocoele*, which is the hollow cavity inside the blastocyst; and the *inner cell mass*, which is a group of approximately 30 cells at one end of the blastocoele. The inner cell mass is used to develop embryonic cell lines through cultivation in laboratory dishes and culture medium.

Only two possible sources of embryonic stem cells exist: leftover embryos from in vitro fertilization procedures (often called "frozen embryos" because of the cryogenic process used to preserve them) or embryos derived from human cloning.

Another viable stem cell source is adult stem cells, also known as somatic stem cells. Specifically, *somatic stem cells* are nonembryonic stem cells not derived from gametes (egg or sperm cells). Sources for nonadult somatic stem cells are amniotic or umbilical chord fluid. In fact, stem cells nearly as powerful as embryonic ones can be found in amniotic fluid. Researchers at Wake Forest have used amniotic stem cells to make muscle, bone, fat, blood vessels, nerves, and liver cells in the laboratory (Coppi et al., 2007).

Adult somatic stem cells are undifferentiated cells found in differentiated tissue that can renew itself and differ-

entiate (with certain limitations) to create the specialized cell types of the tissue from which the cells originated. For example, *hematopoietic stem cells* (undifferentiated cells) in the bone marrow (differentiated tissue) form all the types of blood cells in the body. Another undifferentiated bone marrow stem cell, the *stromal cell*, generates bone, cartilage, fat, and fibrous connective tissue. It is believed that there are many as yet unknown sources of adult stem cells. Known sources for adult stem cells are bone marrow, brain, peripheral blood, blood vessels, skeletal muscle, skin, and liver tissues. However, the number of stem cells in any given tissue is very small, so unlimited somatic stem cell sources do not exist.

Furthermore, scientists do not agree about whether adult stem cells may give rise to cell types other than those of the tissue from which they originate. For example, the stem cells of the bone marrow have already become fairly specialized and are destined to become blood cells of one type or another. These would not be much help in growing new brain or heart cells.

In recent years, experimentation with stem cells has led to the possibility of stem cells from one area being used to create cells in another area, such as liver cells being made to produce insulin, a phenomenon known as *plasticity* (National Institutes of Health, 2006). However, the thinking that has dominated stem cell research is that donated stem cells must be from an earlier pluripotent stage of development, meaning embryonic stem cells (hES).

ADULT VERSUS EMBRYONIC

It is interesting that hES research has received the most attention as the preferred source of cell-based regenerative therapy. As of yet, hES research has not produced even one treatment in one human being. Despite all the media frenzy and promotion, hES cells show promise only to provide cures for neurologic and other diseases.

On the other hand, adult somatic stem cells have produced cures of several diseases. As a prototypic example, hematopoietic stem cell transplantation of stem cells derived from bone marrow or peripheral blood has been around since the 1950s (Thomas, Lochte, Lu, et al., 1957). Recently, adult islet pancreatic cell transplants have enabled juvenile diabetics to be free of insulin shots or pumps (StemCellResearch.org, 2004). Furthermore, research "turning the clock back" on adult stem cells suggests that these cells can be modified with gene therapy to act more like embryonic stem cells (Fox, 2007; Minkel, 2007). In 2007, newfound "satellite stem cells" in muscle tissue may lead to regenerative therapies for muscles damaged from muscular dystrophy (Swaminathan, 2007a) and for treatment of baldness (Swaminathan, 2007b). Table 1 lists current applications of adult stem cell transplant.

2007 Adult Stem Cell Transplantation Procedures in Use

Table 1

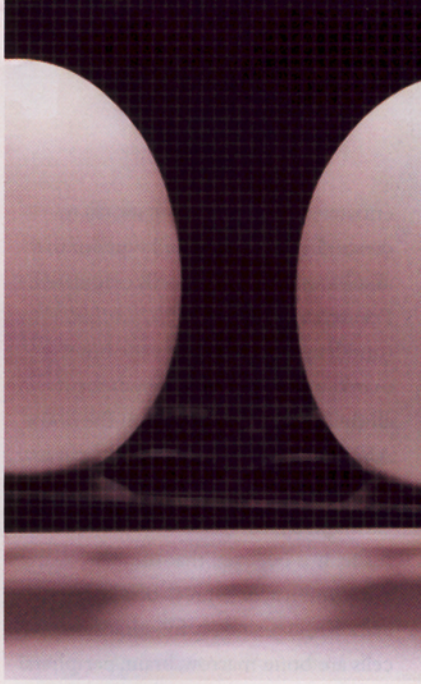
Procedure	Use	Stem Cell Source
Hematopoietic stem cell transplant (HSCT)	Leukemia, hereditary enzyme deficiency (i.e., congenital neutropenia), aplastic anemia, thalassemia major, sickle-cell disease, myelodysplastic syndrome, neuroblastoma, lymphoma, Hodgkin's disease, multiple myeloma, amyloidosis	Autologous or matched allogeneic stem cells from bone marrow, peripheral blood, or umbilical chord blood
Adult pancreatic islet cell transplant (StemCellResearch.org, 2004)	Diabetes mellitus type 1	Cadavers (two or more per transplant)
Vaginal reconstruction (Brown, 2007)	Mayer-Von Rokitansky-Kuster-Hauser syndrome (MRKHS-girls born with no vagina), cancer, other vaginal disorders (This procedure replaces lengthier, painful skin grafting.)	Existing vaginal mucosa from patient

Brown, S. (2007). *Italian doctor builds new more natural vagina.* Reuters News Service. Retrieved June 12, 2007 at http://www.sciam.com/article.cfm?alias=italian-doctor-builds-new.

REALITIES OF STEM CELL TRANSPLANTATION

Although the idea of injecting stem cells into a patient's blood or tissue sounds easy, stem cell transplantation is a risky procedure. To understand what may be involved in future stem cell transplants, we examine an established procedure for hematopoietic stem cell transplantation (HSCT).

The HSCT procedure involves first performing a *conditioning regimen* consisting of chemotherapy, irradiation, or both to destroy naturally occurring hematopoietic cells. Depending on the level of conditioning regimen needed, side effects known as *regimen-related toxicities* accompany the use of chemotherapy and irradiation. Common problems are hepatic veno-occlusive disease, mucositis, and infection. After the procedure, patients



need immunosuppressive agents to suppress graft-versus-host disease and rejection of the transplant, just as with organ transplants. *Graft-versus-host disease*, in which the newly transplanted immune cells attack the recipient's tissues, must be treated with corticosteroids. A newer conditioning regimen known as *nonmyeloablative allogeneic* HSCT uses lower doses of chemotherapy and radiation and does not eradicate all of the bone marrow cells, although high doses of immunosuppressive agents are required in the early stages of treatment. Nonmyeloablative (or "mini") allogeneic transplants, because of their gentler-conditioning regimens, are associated with a lower risk of transplant-related mortality and therefore allow patients considered too high risk for conventional allogeneic HSCT (because of age or other comorbidities) to undergo potentially curative therapy for their disease (Domen, Wagers, & Weissman, 2006).

Because HSCT is associated with a fairly high mortality in the recipient (10% or higher), the procedure is limited to conditions that are themselves essentially life threatening. A newer procedure involving transplantation of adult pancreatic islet cells for the treatment of diabetes mellitus type 1 also requires immunosuppressive therapy (StemCellResearch.org, 2006). These current uses of stem cell transplantation hint at future challenges for stem cell transplantation procedures.

Additionally, the number of adult stem cells in any given tissue is very small, so unlimited somatic stem cell sources do not exist. For example, it takes harvesting from two to three adult cadavers to obtain enough cells to perform an adult islet cell transplant. One advantage of adult stem cells is that an individual's own cells can be harvested for transplantation, thus eliminating the need for immunosuppressive treatment. Otherwise, it is difficult to find acceptable, matched donors.

Another important reality is that although we hear of potentially wonderful uses for embryonic stem cells, to date, no hES treatments have been successful in laboratory or clinical models. In fact, a National Institutes of Health report shows that numerous studies exploring repair of the nervous system with stem cells all have resulted in either failure or less than satisfactory results (not clinically significant or tumors developed) (Panchision, 2006).

Scientists report that stem cells are highly unlikely to offer any type of cure for Alzheimer's.

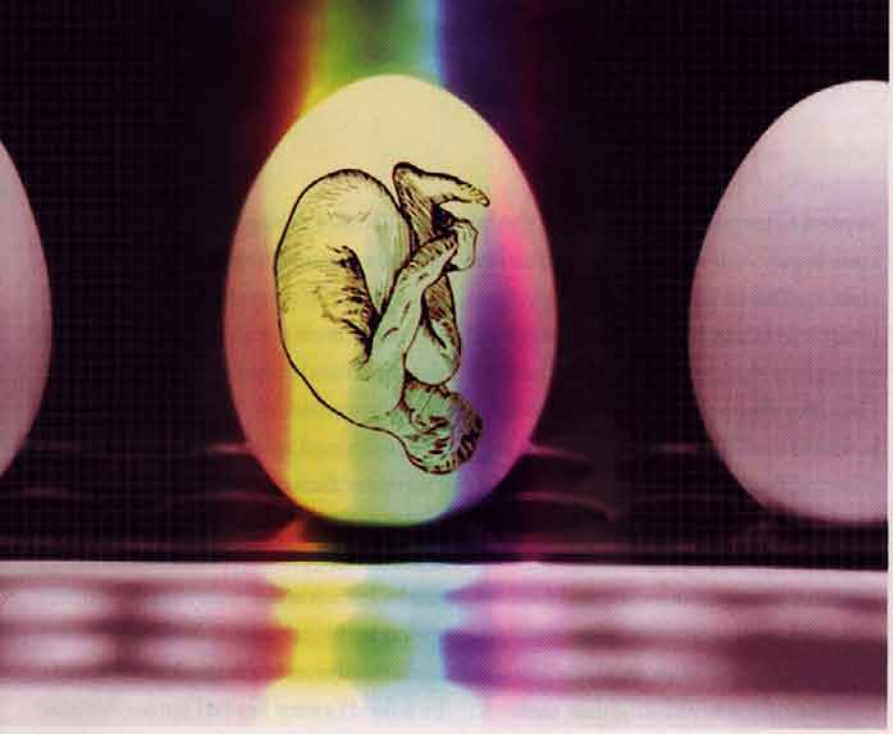
Furthermore, despite the media hype surrounding the treatment of Alzheimer's disease with stem cells, especially after the death in 2004 of former President Ronald Reagan, who suffered from Alzheimer's, scientists report that stem cells are highly unlikely to offer any type of cure for Alzheimer's. Why? Alzheimer's disease entails the loss of huge numbers and varieties of the brain's 100 billion nerve cells, and the countless connections, or synapses, among them. Huntington Potter, a brain researcher at the University of South Florida in Tampa and chief executive of the Johnnie B. Byrd Institute for Alzheimer's Research, explains, "The complex architecture of the brain, the fact that it's a diffuse disease with neuronal loss in numerous places and with synaptic loss, all this is a problem" for any strategy involving cell replacement (Weiss, 2004). Some scientists believe there could be value in stem cell research for Alzheimer's in the laboratory to help us understand basic biologic questions. But this would require creating cloned human embryos using cells taken from Alzheimer's patients—a technique scientists are not willing to perform and politicians are not willing to fund (Weiss, 2004).

A final reality of hES research and any future potential transplantations is that the harvesting of embryonic stem cells destroys human embryos. Therein lies the major ethical dilemma of stem cell research.

ETHICAL DILEMMAS OF hES

In a policy speech delivered to the nation from Crawford, Texas, on August 9, 2001, President Bush described two major ethical issues related to hES research:

> As I thought through this issue, I kept returning to two fundamental questions. First, are the frozen embryos human life and therefore something precious to be protected? And second, if they're going to be destroyed anyway, shouldn't they



be used for a greater good, for research that has the potential to save and improve other lives? (Bush announces his position on stem cell research, 2001).

President Bush has articulated the dual themes of the sanctity of human life (the "sanctity" argument) and the utilitarian rationale for the disposal of embryos already bound for destruction (the "utilitarian" argument).

Many Christians maintain that the sanctity argument is true. That is, they answer "yes" to President Bush's first question. They have fundamental objections to the destruction of embryos to obtain cells because they believe that human personhood begins at the moment of conception. Such writers base personhood and the sanctity of the early embryo on the image of God as described by the Creator in Genesis 1:26–27 (Allen, 2000; Beckwith, 1995; Chire, 2002; Evans, 2000; Feinberg & Feinberg, 1993; Geisler, 1990; Sullivan, 2003). This understanding of the sanctity of life and personhood is central to the discussion of many biomedical ethical issues such as abortion, reproductive technologies, human stem cell research, cloning, assisted suicide, euthanasia, genomics, and resource allocation.

Some have suggested that because embryonic stem cells are *not* derived from eggs fertilized in a woman's body, only from in vitro fertilization, such cells should not be considered "human." But is life determined by where an egg is fertilized? How are embryos developed *in vitro* for stem cell research different from embryos developed *in vitro* for in vitro fertilization (IVF)? If IVF embryos survive, we call them miracles. Others believe that because multiple hES lines can be developed from one embryo, hES cells can be obtained without killing an embryo. But an embryo must be destroyed at some point to start the stem cell line.

MORAL PROTECTION OF EMBRYOS?

If embryos are persons, then morally they should be protected. Killing persons is a moral evil. Are there any legitimate exceptions? Perhaps three come to mind: war, self-defense, and capital punishment. We could, of course, debate the nuances of each. For example, several religious traditions deny there is such a thing as a "just war," whereas others affirm the concept. Self-defense depends on the circumstances, and even in the case of bodily attack, lethal force is not always appropriate. Capital punishment is justified in Scripture (Genesis 9:6), but in practice, there may be racial or economic inequities in the way it is administered.

But none of these exceptions applies to embryonic human beings. This is not war; this is not self-defense; and we certainly cannot claim that embryos have committed a capital offense. Indeed, embryos are the most innocent members of our society.

Who participates in the moral evil of killing embryos? Does moral blame lie merely with the laboratory technician who flushes the cryogenic canister down the drain, or does responsibility for the act include the physician or fertility center director who authorized it? What is the role of the "owners" of the embryos? Whether or not they are the biologic parents, they have the legal power to make decisions about the embryos' fate. Should they be morally culpable as well? One may rightly ask, "Who benefits from the death of this embryo, and should that person bear some of the moral responsibility as an agent of its destruction?" This introduces the idea of moral complicity.

Moral complicity refers to the possible taint of moral guilt attached to a person by association with another who has performed a moral wrong. Taking an example from law, an accomplice or accessory also is culpable to some extent for a crime even if that person does not actually perform the deed (Legal Information Institute, 2007). From a moral perspective, complicity requires that a person be in agreement with the act committed.

"ENDS" VERSUS "MEANS"

The utilitarian argument, the second of President Bush's ethical questions, has not received as much attention in the public debate, yet it is informed by the perspective of moral complicity. Even if it is assumed that frozen embryos will be discarded anyway, complicity considerations make that approach suspect. The utilitarian argument seems to permit research that otherwise would not be ethical, suggesting that the "end" (saving of human life) justifies the "means" (killing of human life).

This conclusion still may be warranted even if the sanctity of embryo life is not alleged. For example, William Fitzpatrick holds to an intermediate view of embryos, not as persons themselves, but as entities wor of "special respect." In justifying cloning for biomedical research, he uses a model of "a deontological constraint that has been overridden by sufficiently compelling special considerations." Nonetheless, he goes on to add rather forcefully:

> [D]espite the all-things-considered justification of proceeding, we are taking what remains an *intrinsically inappropriate* attitude toward the beginning stages of human life. This consideration may eventually be outweighed by others, but it retains some force, which means that the situation is not one we should allow ourselves to grow too comfortable with. (Fitzpatrick, 2003, p. 36, emphasis in the original)

If we then supplement this idea with Christian principles of respect for human life, the issue becomes very clear. A utilitarian calculus used to justify destruction of "leftover" embryos violates any special status for such embryos. Moreover, there is the worrisome possibility of further extending the utilitarian argument beyond frozen embryos to apply the same logic to the debate over human cloning. This rationale that the "ends justify the means" already has been taken to a harsh extreme in the Ukraine. Unbelievably, video footage obtained by the British Broadcasting Company showing postmortem examinations of dismembered babies suggests that healthy newborn babies are being killed to harvest stem cells and feed a flourishing international stem cell trade. Testimony from mothers in the city of Karkiv saying that their healthy newborns were taken by maternity staff and that they were later told the babies had died supports this possibility (Hill, 2006).

FROM EMBRYOS TO CLONED HUMANS

To see how utilitarian justification for destroying embryos could expand to justify other questionable procedures, we must consider the nature of cloning. *Cloning* is the idea of combining genetic material in the laboratory using a procedure technically called "somatic cell nuclear transfer." This technology inserts the diploid genetic material from a body cell (say, the outer skin or the mucous membrane of the mouth) into a human ovum from which the nucleus has been removed. The resulting zygote may then begin to divide.

Popular discussions describe two kinds of proposed human cloning: reproductive and therapeutic. Reproductive cloning has the goal of bringing a new baby into the world. Most responsible parties involved in this debate would support a ban on reproductive cloning. Experience with Dolly the sheep, the first cloned mammal, demonstrated the huge number of attempts required to produce a mammalian clone: Dolly required 434 tries (Pennisi & Vogel, 2000). In other animal cloning attempts, embryos were arrested at the four- or eight-cell stage, but some went on to become highly deformed and abnormal. Dolly herself was not normal, and died eventually of accelerated aging. Because of this "monster factor," most people are understandably reluctant to approve reproductive cloning of human beings, not to mention the many other ethical, moral, and legal questions that it raises.

Yet, if the technological issues could be solved (a very big "if"), many would regard even reproductive cloning as no more onerous than IVF. If fertilization outside of the womb is morally acceptable, then the use of cloning to accomplish this end might be considered merely another form of assisted procreation. Conservative ethicists have grave reservations about this scenario, but at least the "monster factor" would not be in view.

However, an even more frightening possibility is so-called "therapeutic" cloning. This is cloning for the sole purpose of producing stem cells, with no intention of allowing such human beings to remain alive. In fact, as recently proposed in both houses of the U.S. legislature, a ban on reproductive cloning may be passed without an accompanying ban on "therapeutic" cloning. This would amount to a federal mandate that such humans be put to death. Such a law would effectively nullify the Fourteenth Amendment to the U.S. Constitution. More importantly, this would make the state complicit with violating the biblical commandment: "You shall not murder" (Exodus 20:13).

Consider the application of the utilitarian argument in a society that has banned reproductive but not "therapeutic" cloning. The argument

from the present situation: "We should extract cells from leftover embryos in IVF clinics because they are going to be destroyed anyway;" becomes instead: "We should extract cells from cloned embryos because they *must be* destroyed anyway."

In his much-publicized address, President Bush allowed for research on 60 hES cell lines developed from frozen embryos that had already been destroyed. But his decision applied only to those agencies that currently receive federal funding. Indeed, research on human cloning is now active and ongoing in private companies across the United States and around the world. All this is taking place in support of research that has not yet medically helped a single human being.

Yet it appears that the demand for stem cell research is strong, and the general public is impatient with (seemingly) philosophical or metaphysical arguments over entities that many cannot imagine as human persons. Sadly, distortions in the stem cell debate are not being aggressively corrected by scientists, leading to misperceptions and incorrect information (Weiss, 2004). It also is not clear why more public discussion does not focus on ethically permissible research into adult stem cell sources. Because the Bush policy places no restraints on this type of work, it often is funded by the National Institutes of Health.

LONG-TERM IMPLICATIONS

As with most medical procedures, nurses will provide direct patient care to individuals undergoing stem cell transplantation. Nurses will educate and train patients to follow careful immunosuppressive treatment regimens and to be knowledgeable about complications after transplantation. And nurses will need to be prepared to answer questions about stem cell research and transplantation. Christian nurses should be at the front line prepared to respond to ethical questions about hES research and uses.

What is at stake in the stem cell controversy? As an ethical concern, this debate may not seem as immediate as that about abortion or euthanasia, yet the long-term implications are great. At stake is the very way we regard each other, and whom we include in the category of persons. Will our society continue to honor human life in all stages, even the weak and defenseless among us? Or will we succumb to a utilitarian rationale that sacrifices a nameless few for an intangible greater good? The near future will determine whether embryonic human beings are treated as objects that can be discarded or as fellow image bearers created by a loving God.

Web Resources

- International Society for Stem Cell Research: http://www.isscr.org/
- The President's Council on Bioethics—Stem Cells: http://bioethics.gov/topics/stemcells_index.html
- NIH Department of Clinical Bioethics: http://www.bioethics.nih.gov/home/index.shtml
- Center for Bioethics: http://www.cedarville.edu/bioethics

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