Stem Cell Research
The Debate

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Pre-Medical Society

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Neural cells (red and green) derived from human embryonic stem cells. 
ABSTRACT

Recently, stem cell research has become a prominent ethical issue in science and medicine. This report is largely informative, describing what stem cells are, how they are researched, and the role they could potentially play in disease treatment. The arguments for and against embryonic stem cell research are also presented in this report. Embryonic stem cells are pluripotent and are derived from an early embryo in the blastocyst stage. Many consider this type of stem cell research unethical because of the moral debate over the status of the embryo. Researchers believe these cells hold great potential for disease treatment, but embryonic stem cells have not yet been effective in clinical treatments. Adult stem cells are taken directly from adult tissues and are considered multipotent, but may be pluripotent according to the theory of stem cell plasticity. These stem cells, although believed to be more difficult to use, have been used successfully in many clinical treatments. The federal government has provided a compromise with the current stem cell legislation, which is also discussed in this report.

Keywords: medical ethics, embryonic stem cells, adult stem cells, pluripotent, multipotent, stem cell legislation
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Introduction

Stem cell research, one of the most exciting and controversial ethical issues in medicine today, continuously makes headlines with new developments. This topic concerns medical professionals, scientists, ethics forums, and even politicians, but many people do not know what to conclude from the controversy surrounding it. Dr. Elizabeth Crouch¹, a genetics professor of the Biomedical Science Department of Texas A & M University, argues that it is vital that students entering medicine be educated about the ethical issues surrounding stem cell research. She explains:

One of the things that you have to decide as an M.D. particularly surrounding stem cell research, is whether or not you support it, and then once you’ve decided that, you need to know both the pros and the cons so that if you had a patient that you were working with, for example an Alzheimer’s patient … you’d be able to present both sides of the issue, so that they can decide on their own.

Students planning to enter the medical field must be well-informed about this issue so that they can begin to develop their own convictions about medical ethics, specifically regarding the stem cell debate. This report defines stem cells, describes the different types of stem cell research and their potential role in disease therapy, and then presents the ethical controversy surrounding stem cell research.
Part 1: What are stem cells?

**Characteristics**

An understanding of what stem cells are is essential to developing a position regarding the ethics of their use in the treatment of disease. Stem cells are cells at the earliest stage of development. The International Society for Stem Cell Research, a non-profit organization that promotes stem cell education and research\(^2\) defines stem cells as the most basic cells for every body part, from tissues to organs. They have also been creatively described as blank computer chips, each with the ability to be programmed to carry out a specific function in the body.\(^3\)

Stem cells exhibit two definitive characteristics widely accepted by scientists today. First, stem cells have the ability to divide, or reproduce themselves, for long periods of time. Second, they are unspecialized but can become specialized by differentiating, or developing, into individual types of body cells.\(^4\) Stem cells mature into specialized cells that will ultimately develop into tissues and organs when they are in the appropriate environment.\(^3\)

**Types of Stem Cells**

The three different types of stem cells are classified according to their place of origin.

*Embryonic Stem Cells*

The most well known stem cells are embryonic stem (ES) cells. These cells are among the first elements present in the development of a human being. The single-celled *zygote*, created after fertilization, marks the beginning of a human life. It rapidly divides into two cells which divide into two more, and the process continues until about 150 cells are present about five days after conception. These cells are clumped together in a hollow ball, called a *blastocyst*, visualized in Figure 1.1 on the next page. Embryonic stem cells make up the *inner cell mass* of the blastocyst.\(^3\)
Embryonic stem cells are considered to be *pluripotent*, meaning they have the ability to differentiate into cells that will develop into any of the three layers of body tissue (endoderm, mesoderm, and ectoderm) from which all 210 types of body tissues arise.\(^5\) In simpler terms, a pluripotent cell has the capacity to develop into any body cell, such as a nerve cell or a heart muscle cell. Figure 1.2 in Appendix A, taken from a National Institutes of Health report, illustrates this concept.

**Fetal Stem Cells**

The second type of stem cell is called a fetal stem cell. Researchers take these stem cells from aborted fetuses, embryos of about 7-8 weeks of development. Fetal stem cells are embryonic germ cells, the cells programmed to develop into the ovaries or testes of the fetus.\(^3\) These cells, thought to have similar properties to ES cells, may not be able to develop into all types of body cells.\(^3\) Therefore, they are not considered pluripotent. Because stem cell research does not often use fetal stem cells, they will not be discussed in this report.

**Adult Stem Cells**

Stem cells not found in a fetus or an embryo are termed adult stem cells. These cells are found in umbilical cord blood, placenta tissue, blood marrow, fat, tooth pulp, and tissues of the lung, pancreas, brain, breast, and skin.\(^6\) Adult stem cells were previously thought to be multipotent, meaning that they can only differentiate into the same type of tissues from which they are derived. Recently, however, proponents of the “stem cell plasticity” theory have argued that adult stem cells can develop into a variety of specialized tissues.\(^3\) We will discuss examples of this phenomenon later. The two types of stem cells that will be discussed in this report are embryonic and adult stem cells.
**Part 2: Researching Stem Cells**

**Sources of Embryos**

As stated previously, stem cells can be isolated either from embryos, fetal germ cells, or adult tissues.

The embryos used for ES cell research are either donated or cloned. Most of the embryonic stem cells used for research come from *in vitro* fertilization clinics. These clinics grow fertilized embryos *in vitro*, or outside of the body, and implant them into the wall of the uterus when they are in the blastocyst stage. Couples treated for infertility who produce more embryos than they need for implantation can donate their extra embryos for research purposes.\(^7\)

In February of 2004, a human embryo was actually cloned by South Korean scientists for the first time ever. This was for the purpose of extracting stem cells.\(^8\)

**Stem Cell Isolation**

Scientists currently research both embryonic and adult stem cells by isolating stem cell lines. A stem cell line is a collection of stem cells that can continue to divide outside of the body. To isolate stem cells for research, scientists extract adult stem cells from human tissues. Embryonic stem cells, however, are extracted from the blastocyst in a process that destroys the developing embryo. The picture in figure 2.1 captures part of the process of isolating a stem cell from an embryo.

Remarkably, the cells remain undifferentiated for an indefinite period of time, if the right conditions are met. To differentiate the cells into mature, specialized cells, scientists treat them with growth factors and hormones and keep them in a special media in which conditions are similar to those in the human body. They can grow into a wide variety of cell types, such as bone cells, liver cells, brain cells, muscle cells, or kidney cells.\(^9,3\)
The Importance of Stem Cells

Scientists believe that stem cells have the potential to revolutionize the field of medicine because of their unique, undifferentiated state. Scientists anticipate three main applications, including drug research, human development research, and disease treatment.\textsuperscript{7}

Drug Research

Stem cells have the potential to be very helpful in testing different drugs and developing new ones. Scientists could differentiate the cells into specific cell types and study their response to drugs.

Research on Human Development

Scientists could also use stem cells to study the early stages of human development. This kind of research has been nearly impossible in the past, and it would benefit our current understanding of birth defects and infertility.

Disease Treatment

Stem cells have the potential to revolutionize the realm of traditional medicine and disease therapy because of their unique ability to differentiate into various types of tissues. As researcher Catherine Verfaillie\textsuperscript{4} stated, “It was as though they had stumbled upon a packet of magic seeds that, depending on where they were planted, could grow into carrots, broccoli, corn, or cabbage.” Scientists at the International Society for Stem Cell Research explain that stem cells have the capability to replace dysfunctional body cells that are diseased or damaged and incapable of repairing themselves. This process is called cell therapy and is an alternative to organ transplantation. Embryonic, fetal, and adult stem cells are being studied as possible replacements for diseased muscle, nerve, skin, and blood cells.\textsuperscript{3} In theory, any disease caused by damaged or diseased tissue could be cured with stem cell therapy. For example, patients who have damaged heart muscle from a heart attack could theoretically be treated with stem cells that have been programmed to function as heart muscle cells. The process of cultivating the cells for this purpose is diagramed by figure 2.2 in Appendix B. When the stem cells are transplanted into the patient’s heart, the dysfunctional cells are replaced with functional cells.

Stem cell research will supply many promising contributions to the field of medicine and the treatment of disease. Doctors and scientists have seen the great benefits that stem cells appear to offer, and all agree that stem cell research should continue. However, significant debate focuses on whether or not all kinds of stem cell research are moral and ethical.
Part 3: The Ethical Debate

Overview

As we have seen, stem cells can be embryonic, fetal, or adult. The ethical controversy surrounding stem cell research pertains only to embryonic stem cell research. Many people - scientists, doctors, and otherwise - believe it is unethical to harvest embryonic stem cells because embryos are destroyed when stem cell lines are isolated. As Dr. Crouch¹ explains:

…if you’re talking about human embryonic stem cells, then you’re talking about using human embryos, so then you get into the same sort of debate that you get with abortion about when life starts…but really what they’re talking about with stem cells is the 4, 6, 8, 16, or 32 cell stage where it’s a blastocyst. And that’s why it’s even harder to define, because some people are only going to look at that as a ball of cells, and some people are going to look at it as life.

Thus, because of the moral debate about the status of human embryos, the use of ES cells for research and therapy techniques has become an ethical debate.

The Opponents of Embryonic Stem Cell Research

As outlined by the Christian Medical and Dental Association⁴, an organization that believes that personhood begins at conception, the opponents of embryonic stem cell research put forth three fundamental arguments.

Argument 1: Embryonic Stem Cell Research is Immoral

Those who believe ES cell research is immoral hold the conviction that embryos are human beings with the potential for life, and therefore, should have the same rights as humans. Dr. David Stevens¹⁰, the Executive Director of the Christian Medical and Dental Association, recently stated:

Adult human beings are the result of continuous growth that begins at conception. They are human at conception because of their unique genetic code that makes them part of the human species. There is no morally relevant break in their development. Personhood does not depend on having abilities such as the power to reason, self-awareness, a level of intellect, or consciousness.
This group also asserts that personhood does not start when a baby is viable, or able to survive outside of the womb, because viability continues to change based on technology.

**Argument 2: Embryonic Stem Cell Research is Unethical**

The main ethical issue involved in embryonic stem cell research focuses on whether or not embryos should be used as a means to an end. According to utilitarian ethicists, the most ethical action is that which will bring happiness to the greatest number of people. According to this theory, stem cell research would be considered ethical because great advances could be made toward the goal of relieving human suffering. However, the opponents of embryonic stem cell research believe it is unethical to use human embryos to achieve this goal. These people believe that the destruction of human embryos is actually the killing of human beings and argue that even good ends do not justify unethical means. Dr. William Cheshire, a neurologist and bioethicist from The Mayo Clinic, believes that human life is a greater value than scientific advances and argues that the devaluing of the embryo could lead to the devaluing of other lives. He explains:

> More important than the laudable goals of scientific knowledge and technological gain is the basic good of human life itself, through which and for which science exists. It is my view, therefore, that human embryos should be created only for the purposes of procreation, and that applications that rely on destroying nascent human life should be prohibited….To dismiss the humanity of the embryo for the sake of scientific or economic gain would also move us dangerously closer to setting aside the dignity of other vulnerable classes of humanity.

Many religious groups hold the belief that the embryo is a human being from the point of conception. Several of these religions are listed below:

- Hinduism
- Islam
- Buddhism
- Baha’i
- Catholicism
- Eastern Orthodoxy
- Evangelical Lutheran Church
- Southern Baptist Convention
- United Methodist Church
Opponents of ES cell research also remind us that the most important ethical principle in medicine is to “do no harm.” In the Nuremberg Code, a list of regulations were agreed upon after the discovery of the horrible medical experiments that took place in Germany during WWII. The Code stated that “No experiment should be conducted in which there is a priori reason to believe that death or disabling injury should occur.” The issue at hand, then, is whether or not an embryo is a human being. If it is, stem cell research involves its destruction, and this is unethical.

**Argument 3: Embryonic Stem Cell Research Is Illegal**

Presently, federally-funded research in which a human embryo is “destroyed, discarded, or knowingly subjected to risk of injury or death” is illegal in the United States. In August of 2001, President Bush approved research only on about 60 stem cell lines that had already been isolated. The legislation involved in this decision will be discussed in further detail in Part Four.

Those who oppose embryonic stem cell research, however, are avid proponents of adult stem cell research, which has shown much progress in recent years.

**Adult Stem Cell Research**

**The Alternative to Embryonic Stem Cell Research?**

The theory of “stem cell plasticity,” referred to earlier, states that adult stem cells, which have traditionally been considered multipotent, may actually be more like pluripotent stem cells. Research that has been performed on adult stem cells supports this theory, and these cells seem to have more potential than was previously thought. For example, adult stem cells from various different origins in mice have been able to differentiate into heart, lung, intestine, kidney, liver, muscle tissue, and nervous tissue.

Many applications for adult stem cells exist in the treatment of various diseases. In fact, the Christian Medical and Dental Association reports that currently about 15,000 stem cell therapies are available in the U.S., and all of them involve only adult stem cells. For example, adult hematopoietic stem cells, found in bone marrow and blood, are commonly used in cancer treatment.

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**Multipotent stem cells:**

able to differentiate into the type of tissue from which they were derived.

**Pluripotent stem cells:**

able to differentiate into any type of body cell.
treatments. These cells replace patients’ blood cells destroyed by chemotherapy and radiation. Figure 3.1 lists diseases and conditions that have been successfully treated with adult stem cell therapy.

<table>
<thead>
<tr>
<th>Conditions Positively Affected by Stem Cell Therapy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>· Ovarian Cancer</td>
</tr>
<tr>
<td>· Testicular Cancer</td>
</tr>
<tr>
<td>· Multiple Myeloma</td>
</tr>
<tr>
<td>· Neuroblastoma</td>
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<tr>
<td>· Renal Cell Carcinoma</td>
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<tr>
<td>· Brain Tumor</td>
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<tr>
<td>· Kidney Cancer</td>
</tr>
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Sources of information:

Adult stem cells have been used to treat other conditions as well, and potential applications are currently being tested in the laboratory. Several examples are listed below.

**Diabetes:** People with Type 1 diabetes lack islet cells in the pancreas which produce insulin. Insulin is the hormone that regulates the amount of sugar from carbohydrates that enters the bloodstream. In the laboratory, stem cells from the pancreatic duct have been differentiated into islet cells. Diabetic mice that were treated with these cells were no longer diabetic and were able to produce normal amounts of insulin.4,13,15

**Paralysis:** Rats that had been paralyzed for several days were treated with spinal cord stem cells and were able to walk within two weeks.4

**AIDS:** Due to gene therapy, stem cells have been made resistant to the HIV virus and have been able to survive for several months. Progress in this area could allow individuals who have the HIV virus to be made resistant to, and eventually free of, the virus.4 Research in this area is still very limited.
**Heart Tissue Repair:** Bone marrow stem cells and blood stem cells have been used to repair damaged heart muscle in animals and humans. The cells were cultured so that they differentiated into tissue cells, and then they were grown into heart muscle.\(^{14,15}\)

**Parkinson's Disease:** A Parkinson’s patient in California was treated with stem cells that were isolated from his own brain tissue. A year later, his symptoms were reduced by about 80 percent.\(^{15}\)

**Muscular Dystrophy:** Stem cells have been used to renew muscle tissue in mice with muscular dystrophy.\(^{14,4}\)

Researchers at Duke University Medical Center have had amazing successes early this year. They found stem cells in fat tissue that was retrieved by liposuction procedures and were able to culture them so that they differentiated into bone, cartilage, fat, and nerve cells.\(^{16}\) The researchers also took stem cells from umbilical cord blood, caused them to differentiate into vigorous heart and brain cells, and successfully used them to treat children.\(^{17}\)

**Limitations of Adult Stem Cells**

Although evidence suggests that adult stem cells have great potential in the treatment of diseases, it is widely accepted that adult stem cells have two main limitations. First, adult stem cells are more difficult to obtain than ES cells. Dr. Crouch conducted her post-doctorate research with the MD Anderson Cancer Center, and she explained from experience that the main limitation of adult stem cell research is the procedural difficulty of finding and isolating stem cells from animal tissue because there are so many other types of cells present in the tissue as well.\(^1\) She compares the relative difficulty of adult stem cell research (having to find tens of cells out of billions of cells) with that of conducting embryonic stem cell research (finding two or three cells in only a hundred cells).\(^1\) Another limitation is that adult stem cells are harder to grow up in a culture.\(^{7,18}\)

**The Proponents of Embryonic Stem Cell Research**

**Arguments for Embryonic Stem Cell Research**

The scientists and researchers who support embryonic stem cell research are focused on the goal of stem cell research, which is to relieve human suffering.\(^2\) They advocate the usage of embryos from fertilization clinics, most of which are discarded after a patient becomes pregnant. Louis Guenin, a professor of ethics at Harvard Medical School and a member of the International Society for Stem Cell Research, does not ignore the debate over the ethical question about embryonic research, but he explains that it is difficult to know with certainty whether an embryo is actually a human
being. Guenin is a strong proponent of embryonic stem cell research, which he terms “epidosembryo” research, and he argues that embryos have the potential to benefit society:

Nothing can be gained for an epidosembryo by arranging that it perish as waste rather than perish in aid of others. We have a duty, when our means allow, to aid those who suffer. If we spurn epidosembryo research, not one more baby is likely to be born. If we conduct research, we may relieve suffering.

These scientists promote embryonic stem cell research, as opposed to adult stem cell research, because embryonic stem cells are known to be more pluripotent, having a better ability to differentiate into any other tissue type. Another reason is because embryonic stem cells are so much easier to find and use than adult stem cells.

**Limitations of Embryonic Stem Cell Research**

Embryonic stem cells have not yet shown any human treatment benefits, and the two main limitations of ES cell research are outlined by the University of Wisconsin-Madison. The first problem that researchers are trying to overcome is the problem of immune rejection. When embryonic stem cells are injected into a patient for therapy, the body will see them as foreign tissue, and will try to reject them the same way it fights off other antigens. Additional treatments would have to be given to overcome the dangerous side effects. The only way a patient could have embryonic stem cell therapy without the problem of immune rejection would be to clone the patient and use the stem cells from the cloned embryo for the treatment. As mentioned previously, a human embryo was recently cloned in South Korea for the purpose of stem cell research. A stem cell line was isolated from this embryo, but the cells have not yet been used for disease therapy.

Second, researchers need to find a way to control the type of tissue into which stem cells differentiate and how much they grow. Before ES cells are placed into tissue, they must be cultured along with some of the tissue into which they will differentiate. Stem cells divide very rapidly, so one of the dangers involved in injecting the cells back into human tissue is that if any ES cells are still remaining, they could multiply and turn into cancerous tumors.
The first human embryonic stem cells were isolated and cultured in 1998 by the University of Wisconsin-Madison. The six years since then have been full of debate over whether or not this kind of research should continue. Under the Clinton administration, a set of regulations governing the use of ES cells was written. President Bush entered office in 2000, and the stem cell debate became a major focus for the first eight months of the new Administration. Finally, on August 9, 2001, he announced his decision. As summarized by the National Institutes of Health, federal funding would only be given to the embryonic stem cell lines that had been isolated before August 9th, and the lines must meet certain criteria. For example, the embryos must have been created for reproductive purposes, given by a donor who had consented to donating to research, and they could only be donated only if the clinic had enough embryos for its patients’ reproductive needs. According to this guidelines, financially reimbursing donors is also illegal. A portion of President Bush’s August 9th statement on the issue is as follows:

At its core, this issue forces us to confront fundamental questions about the beginnings of life and the ends of science. It lives at a difficult moral intersection, juxtaposing the need to protect life in all its phases with the prospect of saving and improving life in all its stages… While we must devote enormous energy to conquering disease, it is equally important that we pay attention to the moral concerns raised by the new frontier of human embryo stem cell research. Even the most noble ends do not justify any means.

The President’s decision has served to settle the debate, at least for the time being. Those opposed to the research were satisfied that embryonic stem cell researchers would at least be limited in resources and eventually may not be able to continue. Those who support ES cell research were disappointed that they would not have more federal funds to work with, but they were content with the amount of research they would be able to conduct with the isolated lines.

It is possible that the federal limitations have caused this type of research to move at a slower pace therefore limiting successes, but because of the ethical issues that come with ES cell research, it seems that a compromise was necessary.
Great advances are being made in the exciting and controversial research of stem cells. Embryonic stem cell research is considered by many to be unethical, and although these cells have not yet been used effectively in clinical treatments, researchers still believe the pluripotent cells hold great potential for disease treatment. Adult stem cells, on the other hand, while believed to be more difficult to use, have been used successfully in many different treatments, even with human subjects. Figure 4 in Appendix C summarizes the key concepts discussed here.

The goal of all medical efforts is to strive to relieve human suffering while doing no harm. If scientists can use adult stem cells in spite of the complications involved, these cells may provide an ethical alternative to embryonic stem cells. Because of the difficult ethical question regarding the moral status of the human embryo, perhaps it is best to continue to research adult stem cells, which have proven to hold more potential than was originally expected. Adult stem cell research is achieving the goal and providing real therapeutic results, without the destruction of embryos.

Doctors are regularly called upon for advice about issues in medical ethics, and because stem cells seem to hold promise for so many different kinds of diseases, it is probable that one day you will encounter a patient who is a candidate for stem cell treatment. As a pre-medical student, you will eventually need to formulate your own convictions regarding the stem cell debate.
References

1 Crouch, Elizabeth. Dr. Crouch is Assistant Director of the Biomedical Science Department in the College of Veterinary Medicine at Texas A&M University. Date of interview: 2004 Apr 1.


