

**The Ethics and Science of
STEM CELLS**



Paul Szabo, M.P.

It is not the role of scientists to determine the ethical limits to research or the application of genetic knowledge to the delivery of public health. That is the role of legislatures and the public. The job of scientists is to be canaries in the coal mine, saying: **“Hey, there is an issue coming up here, and we should have a full discussion.”**

Dr. Alan Bernstein, President
Canadian Institutes of Health Research
The Globe and Mail - January 27, 2001

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TABLE OF CONTENTS

	INTRODUCTION	4
Chapter 1	LIFE'S GREATEST MIRACLE	7
Chapter 2	STEM CELL SCIENCE	18
Chapter 3	ADVANCES IN RESEARCH	34
Chapter 4	ETHICS AND MORALS	45
Chapter 5	THE GREAT U.S. COMPROMISE	63
Chapter 6	INTERNATIONAL STATUS	82
Chapter 7	CANADA'S LONG ROAD	91
Chapter 8	THE FINAL WORD	112
	GLOSSARY OF TERMS	114
	ABOUT THE AUTHOR	120

INTRODUCTION

Not long ago, the term “genetic engineering” was known only in the mystical research laboratories of the science community. Today, its use is widespread in the context of the gateway to changing virtually every aspect of human life. The frenzy among researchers is testament to that potential and to why so many have characterized this risk-laden quest for virtual immortality as the “Race of the Century.”

A day does not go by without another story about the hope and the potential of stem cells. We have been told that if stem cells reach only their lowest expectations, they will revolutionize health science more than any other development in our history. However, the public and the news media have an exaggerated and inaccurate perception of where biomedicine is, and where it is going.

Most believe that stem cells are already being used to cure a host of ills including Parkinson’s, Alzheimer’s, diabetes and spinal cord injuries. That simply is not the case. On January 15, 2002, the Harvard Medical School announced that their latest research had shown that stem cells relieved symptoms of Parkinson’s disease in rats, but cautioned that they could also cause tumours. If further experiments are successful, it is expected that there could be human trials in about five years.

If we are still five years away from human trials, and who knows how long before therapies are approved for use, why has medical science raised expectations with all the hype and hope rhetoric? If anything, it has distracted attention away from some of the more controversial aspects of this research.

Stem cell research has raised some important social, moral and ethical questions which have not received the same intensity of exposure and discussion. Although that could elevate public apprehension, as has occurred with genetically modified foods, it would clearly put the onus on government to provide full information and the necessary assurances.

If we pursue genetic engineering, will we be able to control it to ensure that it is safe and not exploited in unintended ways? Tragedies such as thalidomide and its generation of limbless children remind us that biomedical research is not infallible. Should we not expect potential break-throughs to be approached with due caution and the highest ethical standards under the scrutiny of a credible regulatory framework?

Illness, disease and death are parts of life that impact a society in many ways. Our challenge is therefore to find a balance between the ability of medical science to enhance our lives with the need to protect our individual and collective interests.

The objective of this book is to provide a foundation of information on what has arguably become the debate of the millennium. It looks at the complexities of procreation; explains the science of stem cells; highlights what research has been done to date; and presents the related moral and ethical concerns. It also summarizes U.S. and other international developments and examines Canada's long road to legislation.

Now legislatures and the public must take up the debate to determine the ethical limits to research and the application of genetic knowledge to the delivery of public health.

Paul Szabo, M.P.
January 21, 2002

QUOTABLE QUOTES

Our technological capability today outpaces the science fiction of only a few years ago. Present-day advances in science and technology now touch every stage of our lives and penetrate to the very origins of human beings.

Dr. Wilbert J. Keon, Senate of Canada

We hold life in the palm of our collective human hands in a way that no humans have ever held it. We can change the essence of human life itself ... the outcome of 800 million years of evolution.

**Dr. Margaret Somerville, Acting Director,
McGill Centre for Medicine Ethics and Law**

The commercial potential of cell-based therapies is going to be huge. We are obtaining stem cell lines from Australia under an agreement to use them for research purposes only.

**Stewart Howe,
Toronto Hospital for Sick Children**

2001 was a very busy year. It was a year that highlighted the growing disconnect between scientific fact and policy development. Science policy is increasingly based on gut reactions. Instead of nuanced and informed discussion of regulatory challenges created by the genetic revolution, we got little more than a recitation of unsupported bioethics clichés.

**Timothy Caulfield,
Canadian Research Chair in Health Law and Policy,
University of Alberta**

Chapter 1

LIFE'S GREATEST MIRACLE

In simple terms, stem cell therapy is described as a process of extracting cells from a source, modifying certain traits and using them to cure a disease or grow an organ for transplant. If it sounds too good to be true, caution can be a good thing.

Science can emulate the steps it observes but it cannot exactly replicate the subtleties of nature. To appreciate stem cell issues, they need to be considered in the context of the complexity of the reproductive process. Only then can one grasp the enormity of the challenge that science has undertaken and the degree of risk that something can go wrong. It takes no skill, training or talent to procreate. In fact 50 percent of pregnancies are unplanned. It's so simple that scientists can replicate fertilization by a microscopic procedure of injecting sperm into an egg. Does it matter how an egg is fertilized? Apparently it does.

In November 2001, PBS sponsored a Nova film entitled "Life's Greatest Miracle" which makes the case of just how complex the reproductive process is. This chapter presents the biological detail from that program.

Around the world about 365,000 babies are conceived every day. As ordinary as it may seem, creating a new human being is no simple feat. From a single cell, we build a body that has 100 trillion cells. That body has hundreds of different kinds of tissues and dozens of organs including a brain that allows us to do remarkable things. Today we know much more about how this really happens.

New technology allows us to look into the womb, into a cell and virtually into the essence of life itself. Not only can we see what's happening, but we are beginning to see the forces that build the embryo and the molecules that drive this remarkable change.

Without even thinking about it, almost all adults are busy trying to reproduce. They can't help themselves. The urge to procreate is a fundamental part of life, not just for us, but for all life. Scientists believe that this universal urge is due to DNA (Deoxyribonucleic Acid) which is the genetic material, in the form of a double helix or spiral contained in the chromosomes with codes for hereditary characteristics. DNA is the molecule that carries our genes and the chemical instructions for building our bodies and keeping us alive.

The important feature of DNA is that it is very good at making copies of itself. Those copies can get passed on to a new generation in a couple of ways. Bacteria grow by making exact replicas. Through this cloning, each new bacterium has exactly the same DNA. In humans, this process can also be dangerous.

If humans were all clones, everyone would have the exact same immune system which means that one successful parasite could wipe us all out. Fortunately with sexual reproduction, two individuals each provide some DNA. Most animals put it into sperm or eggs and if the two get together, a new being will be created that is different from each of its parents and everybody else as well.

Inside a man's testicle you would find that it is packed with tiny tubes coiled into bundles. Stretched out they could cover half a mile. Inside all of this tubing, the average man is producing about 1,000 new sperm every second. That's about 100 million new sperm every day and more than two trillion over a lifetime. Even

more astounding is that every sperm is one-of-a-kind carrying a unique genetic package. To understand how one person can produce so many different combinations of genes, we need to look at the very special way that sperm and eggs are produced. This process is called “meiosis”.

In almost every cell of your body, you have 30,000 or more different genes spread out on very long strands of DNA called “chromosomes”. Most cells have two versions of every gene for a total of 46 chromosomes. Exactly half of those, 23, came from the female, and 23 came from the male. They come in pairs where the partners are very similar but not quite the same and the only time they get together is during meiosis.

Inside a testicle, each chromosome makes an exact copy of itself keeping attached at one point creating an X-shape. Then the chromosome partners get together and cling so tightly that clusters of genes actually get exchange between them. The cell then divides twice, each time pulling the pairs apart. The final result is a sperm or an egg cell with 23 chromosomes or half the normal number. By itself, the cell is incomplete but still holds incredible promise because every chromosome now carries a combination of genes that has never existed before.

All this gene shuffling means that within a single species, there can be an enormous amount of diversity which improves the odds that someone will survive to create a new generation. That is the common goal of all life species.

While men are constantly producing sperm, a woman created all her eggs when she was a fetus in her mother’s womb. Within a couple of months, a female fetus creates several million eggs and then they begin to die. By age 30, a woman may only have a few thousand eggs remaining but this is not a problem because inside

an ovary, its quality, not quantity that counts. Every month, one of a woman's two ovaries selects an immature egg cell for special attention.

Hundreds of support cells tend the egg, feeding it until it grows fat. When it is ready, the egg, along with its helpers, leave the ovary and migrate to the fallopian tube which leads to the uterus. The egg has everything it needs to start a new life except the DNA from a sperm.

At the height of sexual excitement of a man, millions of sperm are squeezed out of storage through the penis. It's only about a teaspoon of liquid but it typically contains about 300 million sperm. Since a woman's vagina is acidic, the sperm must escape or die.

Even in healthy men, 60 percent of the sperm can be less than perfect. Sperm that escape move on their journey and their success, to a great extent, is controlled by the woman's body and even the egg itself.

For a few days each month around ovulation, the cervix, which is the passageway to the uterus, forms tiny channels that guide the sperm through. In the fallopian tube, some sperm can get caught up in the cilia or fibres lining the tube. It's here that chemicals in the woman's body alter the sperm's outer coating. Only those sperm that are altered will move on over the course of a few days. At any given time, only a couple of hundred sperm will actually move on.

Further along the tube, the sperm will find the egg still surrounded by its support cells which will only let some of the remaining sperm through. The egg itself is encased in a thick protein shell called the “zona”. To fertilize the egg, the sperm must break through the zona but this cannot be done by brute force alone. In fact the egg decides which sperm will be allowed to enter.

Proteins protruding from the sperm’s cap must hook up precisely with a set of proteins on the egg’s surface. If they match, the sperm is held fast and undergoes a dramatic transformation. It sheds its outer coating, releasing powerful enzymes that dissolve a hole in the zona allowing the sperm to push its way through. The sperm still does not thrust its way into the egg itself. Rather, the membranes of the two cells fuse and the egg draws the entire contents of the sperm inside.

Once the sperm and egg get together, their agenda is to create a viable embryo. However, their chances aren’t great. It is estimated that more than 50 percent of all fertilized eggs fail to develop.

In order to survive, the egg has a lot of work to do. First, it orders the zona to lock out all other sperm. Then the egg expels half of its chromosomes into a tiny pouch called a “polar body”. The sperm then releases its 23 chromosomes which join with the chromosomes of the egg and then the cell divides.

By this time, 24 hours have passed and the fertilized egg is moving down the fallopian tube towards the uterus. Every few hours, the cells divide again gradually building the blocks needed to construct an embryo. On rare occasions, the tiny cluster of cells splits into two groups and creates two embryos

- identical twins. However, most of the time, the cells stick together. They must complete just the right number of cell divisions before they arrive in the uterus about five days after fertilization. What started as a large single cell has divided into just over 100 much smaller cells but they are still trapped within the hard shell of the zona.

Now called a “blastocyst”, the bundle of cells must break out of the zona and find a source of nourishment. At the beginning of the sixth day, it releases an enzyme that eats through the zona and the ball cell squeezes out landing on the blood-rich lining of the mother’s uterus.

The blastocyst is still in grave danger however. The mother’s immune system could consider it to be a foreign invader and the white blood cells could swarm in to devour it. In self-defense, the ball of cells produces several chemicals that suppress the mother’s immune system inside the uterus. Searching for food and oxygen, cells from the blastocyst reach down and burrow into the surrounding tissue eventually pulling the entire bundle into the uterine lining.

Two weeks after conception, when the blastocyst is about the size of a poppy seed, the cells start to organize themselves into an embryo. This process is called “gastrulation”. The blastocyst creates two oblong bubbles one on top of the other. Sandwiched between them is a thin a layer of cells. These are the cells which one day may become a baby.

At the beginning of gastrulation, some cells begin moving toward the center. Then they dive downwards, creating a new, lower layer. More cells plunge through, squeezing in between, forming a third

layer. The cells in the three layers may not look different, but for each layer, a very different future lies ahead.

The lower cells are destined to form structures like the lungs, liver, and the lining of the digestive tract. The middle layer will form the heart, muscles, bones and blood. Finally, the top layer will create the nervous system, including the spinal cord and brain as well as the outer covering of skin and eventually hair. This is a human embryo three weeks after fertilization. Less than a 10th of an inch long, its neural tube, the beginning of the nervous system, is already in place.

A couple of days later, the top of the tube is bulging outwards on its way to becoming a brain. With the primitive brain cells exposed, we can see some are sending feelers, making connections to other cells. These vital neural connections will continue to form years after birth.

As the days pass, changes proceed at a rapid pace throughout the embryo. Everywhere cells are multiplying and on the move. Some reach out to one another forming blood vessels. A heart begins to beat. As the embryo lengthens, the precursor to the backbone forms. Groups of cells bulge out on the sides, the beginnings of arms and legs. This is the embryo four and a half weeks after fertilization. It is only about a fifth of an inch long. The primitive backbone now curls into a tail which will disappear in a few weeks. A large brain is developing and on the side of the head an eye is forming.

How does this happen? How does the embryo transform itself from a blob of cells into different tissues and organs and finally into a functional baby? The secret lies in your genes - in your DNA.

Inside, almost every cell in your body, you have the same 46 chromosomes, carrying the same genes. But not all the cells in your body are the same. Nerve cells, blood cells, cells lining your intestine, all look different and all have different jobs. Each of the cells has different groups of genes turned on. When a gene is turned on, it tells the cell to construct a particular protein.

Proteins are the molecules that build your body - like collagen, a fibre that makes up much of your skin, tendons, and bones or keratin in your hair. Crystallin is the protein that helps make the lens of your eye clear. Some proteins also do work. Actin and myosin move muscle fibres and hemoglobin in the blood carries oxygen from the lungs to the rest of the body.

When an embryo is developing, how does a cell turn on the right set of genes and create the right proteins? Part of the answer is location. Once the basic body plan is established, with a head on one end, back and front and left and right sides, cells seem to know exactly where they are and what they're supposed to become. This is because cells talk to each other in the form of chemical messages. Chemicals in one cell can trigger a reaction in the cell next door that can be spread to the cell's nucleus and turn genes on or off.

If all the DNA in a single cell were stretched out, it would be about 6 ft. long but it is all wound up very tightly coiled around balls of protein. For a gene to be turned on, something has to come in and loosen up the right section. Then the cell's machinery can latch on and read the DNA, the first step on a long road to building the protein. Those molecules that can turn genes on play a key role in every aspect of development including the process that transforms the embryo into a boy or girl.

In the seven week-old embryo, boys and girls look exactly alike. Even on the inside there are two gonads which could become testicles or ovaries and there are two sets of tubes, one in case it's a boy, the other for a girl.

There is one way to tell the difference. Just look at the chromosomes in a cell from the embryo. One pair among the 23 determines sex. An embryo with two X chromosomes usually becomes a girl. If one of those X's is a Y, it will most likely be a boy.

Recently, scientists came up with a good theory of how this works. There are only about 30 genes on the Y chromosome. One of them is called SRY. This gene seems to function just once in a lifetime, late in the sixth week of embryonic development. This occurs only in one place, the gonad. SRY turns on for a day or two and the cells churn out its protein. In that short time, SRY sets up the chemical chain reaction, turning on other genes, eventually turning the gonads into testicles, which begin to make testosterone.

Testosterone travels throughout the body. If it reaches the genitals then the cells here will build the penis. But if there are two X chromosomes and no Y, different genes get turned on and the gonads become ovaries. The embryo becomes a baby girl. This is the power of genes, creating cascades of chemical reactions, defining the form and function of all cells in your body.

Sometimes genes send the message to multiply and grow as with the arm and leg buds. Sometimes the message is to die, as it is a few days later to the cells between the fingers. As the weeks pass, the embryo's genes send billions of individual messages, constructing new kinds of cells and building organs and limbs.

Two months after fertilization, the embryo is now called a fetus. Almost all of its organs are in place though they're not working yet. The whole fetus is just over an inch long and weighs less than a third of an ounce. Over the next six and a half months, it will continue to develop in miraculous ways and grow almost 400 times larger in preparation for birth.

We are all unique from conception with many set predispositions. Some are strong and some are weak and while science seeks to heal, it should do no harm. Therein lies the argument that life's greatest miracle must be given the highest respect both by science and by mankind.

QUOTABLE QUOTES

I think Bush was absolutely right that embryonic stem cell research is at the leading edge of a series of moral hazards. It is important that we achieve our benefits in medicine and health without undermining what is humanly decent and dignified. Even if cloning is rarely undertaken, a society in which it is tolerated, is no longer the same society, any more than is a society that permits incest or cannibalism or slavery on even a small scale. It is a society that has forgotten how to shudder, that rationalizes away the abominable.

Dr. Leon Kass, Chair, President's Council on Bioethics

Sooner or later, we're going to read about the world's first cloned baby. Designer babies will become commonplace one day, at first engineered to be free from inherited diseases, soon afterward sculpted scientifically to make them more beautiful, more brainy, more athletic.

Columnist Richard Gwyn, Toronto Star, July 29, 2001

The embryonic stem cells used in the procedure (to treat a 52 year-old man who was suffering from Parkinson's disease) did not develop quite as they had hoped, and in fact (during the autopsy), they found bone and hair follicles, not tissue, growing in the man's brain.

Author Debi Vinnedge, Testimony to U.S. Senate hearings on stem cell research, April 26, 2000

Did your parents destroy your life? Were they alcoholic, child-beating molesters? Did you never have a chance? Interestingly, human cloning allows you the opportunity to participate in choosing the parents for your clone.

Human Cloning Foundation WEB site

Chapter 2

STEM CELL SCIENCE

What was once the subject of science fiction not so long ago is now reality. Test tube babies were just experimental research but today, in vitro fertilization (IVF) is a common procedure to assist those couples with infertility problems. Harvest eggs from a woman; fertilize them in a glass dish; implant the embryos in the mother's womb; and a child is born. It all seems so simple but there is a troubling ethical concern.

The IVF procedure creates many fertilized embryos. Those not needed for the procedure are frozen for future use by the couple or with their consent, the embryos have been used for research purposes. Addressing infertility is one matter but experimenting with a human embryo is quite another.

Is there really any difference if, for research purposes, a fertilized embryo was removed from a woman before it implanted in the mother's uterus? The issue is a matter of **when does life begin and should research, which destroys those human embryos, be permitted.**

The debate on this issue was heightened with the November 25th, 2001 announcement by Advanced Cell Technology Inc. that they had cloned a human embryo. As well, the question of legal status, which historically had focussed on the fetus and abortion, was now being applied to the fertilized embryo which has the viability to become a human life. This surely weighed heavily on President Bush when he made his decision to restrict funding of embryonic

research only to those embryos where the life and death decision had already been made.

Stem cells have become the focus of most discussion on reproductive technologies and it is essential that we understand why they have drawn this attention. Embryos created in the laboratory are not only used for reproduction but also for research. Science has now discovered certain cells, called stem cells, which are slowly demonstrating that they have great potential.

In May 2000, the U.S. National Institutes of Health published a primer to present background information on stem cells. While it appears to have been widely adopted for training, there are some differences from some of the more current descriptions.

In any event, they describe stem cells as having the ability to divide for indefinite periods in culture and to give rise to specialized cells. They are best described in the context of normal human development.

Human development begins when a sperm fertilizes an egg and creates a cell that has the potential to form an entire organism. This fertilized egg is *totipotent*, meaning that its potential is total. In the first hours after fertilization, the cell divides into identical totipotent cells. This means that either one of the cells, if placed into a woman's uterus, has the potential to develop into a fetus. In fact, identical twins develop when two totipotent cells separate and develop into two individual, genetically identical human beings.

Approximately four days after fertilization and after several cycles of cell division, these totipotent cells begin to specialize, forming a hollow sphere of cells, called a blastocyst. The blastocyst has an outer layer of cells and inside the hollow sphere, there is a cluster of cells called the inner cell mass.

The outer layer of cells will go on to form the placenta and other supporting tissues needed for fetal development in the uterus. The inner cell mass cells will go on to form virtually all of the tissues of the human body. Although the inner cell mass cells can form virtually every type of cell found in the human body, they cannot form an organism because they are unable to give rise to the placenta and supporting tissues necessary for development in the human uterus.

These inner cell mass cells are *pluripotent* - they can give rise to many types of cells but not all types of cells necessary for fetal development. Because the potential is not total, they are not totipotent and they are not embryos. In fact, if an inner cell mass cell were placed into a woman's uterus, it would not develop into a fetus.

The pluripotent stem cells undergo further specialization into stem cells that are committed to give rise to cells that have a particular function. Examples of this include blood stem cells which give rise to red blood cells, white blood cells and platelets; and skin stem cells that give rise to the various types of skin cells. These more specialized stem cells are called *multipotent* or as researchers have dubbed them, *adult stem cells*. Every somatic or bodily cell in a human being possesses the full genetic code, the DNA, of our entire makeup.

There are a variety of sources of stem cells. Embryonic stem cells which are harvested from pre-implantation embryos; embryonic germ cells which are found in the primordial reproductive cells of the developing human being; adult stem cells which exist naturally in the various organs and tissues of the body such as bone marrow, in the brain and in fat tissue; cells from umbilical cord blood and placenta tissue and from fetal bone marrow after miscarriage; and

finally from human embryos created asexually by “somatic cell nuclear transfer” or similar “therapeutic cloning” techniques.

Private research on stem cells is reported to have developed more than 60 genetically diverse stem cell lines from embryos that have already been destroyed. An embryonic cell line starts as a cluster of cells, each able to evolve into any body tissue. These cells have the ability to divide virtually forever. In effect, the cell “line” is endless. Properly cultured with special proteins, the new cells could evolve into heart, muscle, liver, brain and other tissue.

Researchers believe that these fresh cells could be injected into patients to boost or repair ailing organs. But not all embryonic stem cell lines are the same. Since they come from different embryos, they have fundamental genetic differences. As with organ transplants, therapeutic stem cells would have to be compatible with the immune system of the receiving patient. Without this capability, the body rejects the curative cells, just as an incompatible kidney or heart can be rejected in an organ transplant.

Adult stem cells are specialized cells that are capable of dividing and making more of themselves. There are two kinds of adult human stem cells, germ-line and somatic. The germ-line cells replicate ova and sperm. Somatic cells replicate all other cells of the body. Initially it was thought that adult stem cells had limited ability to become other types of cells but research has now shown that they can differentiate to create various cell types.

In the blood, for example, red blood cells carry oxygen and white blood cells fight infections. Both cell types come from a haematopoietic stem cell which resides largely in the bone marrow and produces a constant supply of blood cells. Those blood cells have to be renewed constantly. Skin is another tissue that also has to be renewed constantly and there are stem cells below the surface

of the skin that regenerate it. Other tissues, such as brain, muscle, liver and kidney are relatively static tissues. They don't undergo a lot of constant renewal but they still have stem cells and those stem cells are involved in regeneration and repair as often as needed.

Adult stem cells that are multipotent include cells from the brain, fat, skin, blood and bone marrow. The Canadian Institutes of Health Research maintains that adult stem cells are not as useful as embryonic stem cells. However, recent evidence clearly shows that adult stem cells have a broader potency than first thought. Some have suggested that adult stem cells may prove safer and more flexible than fetal cells because adult cells have been shown to travel to areas needing repair whereas fetal stem cells remain where they are injected.

In addition, because the patient can often donate their own adult stem cells for treatment, the immune system will not reject them. On the other hand, a person treated with embryonic stem cells would likely have to take anti-rejection drugs for the rest of their life.

The results of adult stem cell research to date have been very encouraging. The following are a few examples of the potential of some of that progress:

- Researchers have been able to extract adult stem cells from bone marrow, blood, brain, muscle and skin tissue and have been able to turn them into fat, bone, cartilage, muscle, blood, nerve and liver cells.
- The Salk Institute in California was able to extract useful brain cells from donor cadavers 10 hours to three days after

death and was able to grow them into a number of different nervous system cells.

- Italy's Stem Cell Research Institute took stem cells from an adult brain and turned them into skeletal muscle.
- McGill University researchers have injected bone marrow stem cells directly into the heart which developed into heart muscle cells.
- Researchers from the University of Pittsburgh turned stem cells from fat into healthy cartilage, muscle and bones.
- On December 12th, 2001, researchers in Montreal discovered that a stem cell found in adult bone marrow does not cause rejection by a recipient's immune system. They reported that the cells only seem to go to damaged areas once injected. They turned into heart muscle, blood vessels and fibrous tissue.
- In July 2001, British scientists reported that stem cells from adult bone marrow are capable of turning into mature kidney cells. These cells could be used to replenish kidney cells lost by injury and there would be much less complication with the kidneys rejecting the new cells.
- In August 2001, researchers from the Walter and Eliza Hall Institute in Australia identified and isolated adult stem cells from the brain which can develop into new nerve cells. It has been proved that a single stem cell could give rise to thousands of new neurons or muscle cells.
- In August 2001, scientists at the University of Dusseldorf Cardiac Clinic achieved a world first by using bone marrow

stem cells to heal a man's heart. They extracted the cells from the patient's pelvis and injected them into his coronary arteries. The stem cells migrated to areas damaged by the heart attack and turned them into healthy muscle cells which began to beat.

- On August 9, 2001, doctors at Northwestern Memorial Hospital in Chicago reported that adult stem cells extracted from the blood of two Crohns patients have been used to rebuild their faulty immune systems.
- U.K. research published in the "Stroke Journal" reports that stem cells transplanted from a patient's own body will be able to aid in the recovery of those who suffered strokes. **They report that the cells are more effective than cells from embryos because they are selective and they travel to the part of the brain in need of repair. The cells from embryos lack this ability.**

Adult stem cell research not only has shown great promise, but their clinical trials and some clinical applications are well advanced unlike the situation for the more controversial embryonic stem cells.

Another description of embryonic stem comes from Dr. John Shea. He states that the human embryo, from the moment of cleavage of the zygote into two cells until, at the latest, the 18th to 19th day after conception, contain cells called *blastomeres* that are totipotent. This means that if a cell, or group of cells, spontaneously become separated from the embryo, or are deliberately separated from the embryo, those cells have the natural tendency and capacity to revert to being a human zygote, another human being. (This ability to become an embryo was confirmed in

a research paper on August 3, 2001 by Dr. Dianne Irving, a world-renowned bioethicist and former biochemist with the U.S. National Institutes of Health).

This capacity is due to a process called regulation, a natural tendency or property inherent in the separated cells or group of cells. Any separated blastomere may die, become a new zygote (human being) or be cloned to produce specific tissues. This cloning may not only kill the embryo from which the blastomere was removed but also the newly formed embryo itself.

The blastomeres which are separated but do not die or become a human embryo are referred to by researchers as embryonic stem cells and they have the capability of making virtually any cell type or any tissue through a therapeutic cloning process. Cells with this ability are called pluripotent.

In 1998 scientists were able to grow human embryonic stem cells in culture and discovered that adult stem cells could be used to make different tissues. In other words, stem cells taken from the bone marrow, which is normally involved in making blood, might be able to make muscle; or stem cell from a muscle, which is normally there to make muscle, might be able to make blood cells if you put it into the bone marrow.

Stem cells in the brain, that normally make neurons, were able to make blood - and stem cells from the blood could make neurons for the brain. This was a very important discovery because if you could take stem cells from an individual and repair a different tissue in the same individual, then you eliminate all the problems of immune-system rejection we normally face with any kind of tissue or cell transplant. These discoveries are the reason that there has been such a frenzy of research in the area of stem cells.

Embryonic stem cells can be grown and differentiated in tissue culture to produce very large numbers of cells for transplant or tissue engineering. Adult stem cells by contrast cannot be easily grown in tissue culture but they can be introduced in small numbers into the blood system where they can home in on areas of damage and participate in the regeneration of tissue. This kind of treatment has been going on for at least two decades. A bone marrow transplant is exactly that - the transplant of adult stem cells to reconstitute the bone marrow system.

Although there has been a great deal of hype about the potential of embryonic stem cells, there is equally a great deal of apprehension about the unknown. Genetic engineering, cloning and cell research have garnered much publicity about their potential and whether there has been evidence that the apprehension may be well founded.

On July 6th, 2001, a new study published in the journal “Science” reported that **embryonic stem cells used in cloning mice often result in severe abnormalities**. Cloned mice created with embryonic stem cells may look normal but often have subtle abnormalities. In humans, these flaws could affect personality, intelligence and other human attributes.

Researchers found that stem cells might carry unexpected risks when used to reproduce organisms. The problem did not lie with the process but rather in the makeup of **the embryonic stem cells which have been found to be extremely unstable in laboratory cultures**. The genes themselves were not at fault. However, the embryonic stem cells lost the tags that were supposed to tell the genes whether to turn on or off during development.

The research has shown that the development of cells to form tissues and organs at the right place at the right time is an extremely complex process. If one cell goes awry at the wrong time or place, the resulting organism can be seriously flawed.

Stem cells reveal natural biological variations. Studies in mice have demonstrated that the ability of a mouse to accept stem cells varies given this natural biological variation. There is a possibility that some embryonic stem cells would create immunogenic reactions in adults.

Researchers have found it **extremely difficult to control cell growth during embryonic stem cell research**. As a consequence, some researchers are concluding that tissue specific stem cells harvested from this source may prove to be far more effective than the pluripotent stem cells harvested from human embryos.

One of the researchers commented that embryonic stem cells are so difficult to work with, that the potential that they would explode into a cancerous mass after a stem cell transplant might turn out to be the Pandora's box of stem cell research. The results of the study lend strong support to the view that government should only support research that is ethical and shows the most promise such as adult stem cell research. The same view was expressed during the hearings before the House of Commons Standing Committee on Health and was strongly supported in the final Committee report.

The Committee also had some concerns about the infertility industry and the procedure of in vitro fertilization (IVF). IVF has been used for many years to help couples with infertility problems. The procedure involves fertilizing a woman's egg in a laboratory setting with sperm from the spouse or another donor. This creates an embryo which is implanted into the womb of the mother. To

obtain the eggs, the patient is given hormone treatments which causes her to hyper ovulate thereby producing a number of eggs which are harvested from her body.

The normal practice is to fertilize as many eggs as possible and to freeze and store the spare embryos for future use or for research. It is often suggested that unwanted or discarded frozen embryos used in research would otherwise have been destroyed. This is not entirely accurate. There are embryo adoption options such as the Snowflake program operating in California.

It is interesting to note that sperm and embryos can be frozen for future use but science has still not found a way to safely freeze eggs without damaging them. If eggs could be frozen, there would be no need to create spare embryos. Sperm and eggs required for an IVF procedure could be prepared for that procedure only.

This issue was raised during the hearings held by the House of Commons Standing Committee on Health, and was included in their final report. It's hard to believe that embryos can be safely frozen, but eggs cannot. If they could be frozen, this would have great consequences since it would deprive researchers of the most important source of human embryos for research purposes.

The U.S. is also concerned about this issue. On November 29, 2001, President Bush raised a red flag for advocates of in vitro fertilization when he authorized his new Commission on Bioethics to examine, among other things, the ethics of the reproductive procedure.

The chair of the President's Council on Bioethics is Leon Kass who is a bioethicist from the University of Chicago. While he is in favour of using IVF for the treatment of infertility for married

couples, he has expressed concern about the unethical experimentation on the unborn and the potential risk for the unborn child.

The American Society of Reproductive Medicine has recorded about 100,000 U.S. births - 250,000 worldwide - as a result of in vitro fertilization since the procedure produced the world's first test-tube baby in England in 1978. One fact that is rarely mentioned is that at least 500,000 live human embryos had to be sacrificed in the attempts to have those 250,000 children born.

The IVF procedure normally involves placing two or more embryos in the womb to ensure the survival of at least one child. If more than one child survives implantation, the recommended treatment for multiple pregnancies is often **fetal reduction which is killing any unwanted fetus**. It is also estimated that there are over 100,000 embryos still in frozen storage.

How long embryos can be kept in a frozen state without deteriorating is not known for certain but estimates range from 2 to 5 years. Fertility clinics that perform IVF are the primary source of embryos that scientists use for the study of stem cells and other experimentation.

Specifically, the executive order of the President states that the Council shall advise the President on bioethical issues that may emerge as a consequence of advances in biomedical science and technology. In connection with its advisory role, the mission of the council includes the following functions:

1. To undertake a fundamental inquiry into the human and moral significance of developments in biomedical and behavioural science and technology;

2. To explore specific ethical and policy questions related to these developments;
3. To provide a forum for a national discussion on bioethical issues;
4. To facilitate a greater understanding of bioethical issues; and
5. To explore possibilities for useful international collaboration on bioethical issues.

The order goes on to authorize the Council to study ethical issues connected with specific technological activities such as embryo and stem cell research, assisted reproduction, cloning, uses of knowledge and techniques derived from human genetics or the neurosciences and end of life issues.

The Council may also study progress on ethical and social issues not tied to a specific technology such as: questions regarding the protection of human subjects in research; the appropriate uses of biomedical technologies; the moral implications of biomedical technologies; and the consequences of limiting scientific research. The research community fully expects the council to take a critical look at the IVF procedure and how it might continue to fulfil its purpose without destroying human embryos.

Undoubtedly the President's Council will also be following the cloning issue very closely considering the high level of interest by privately funded research to pursue this darker side of scientific search. Cloning is generally understood to be the intentional creation of one or more genetically identical individuals. **However,**

you will also hear references to cloning in regard to embryonic stem cell research.

The process usually refers to a form of asexual reproduction in which the genome from a cell of an individual is used to generate one or more genetically identical individuals. Cloning technology can be used to generate early embryos that are genetic copies. Instead of making live born clones, you can stop the embryos at the blastocyst stage and harvest stem cells which is referred to as “**therapeutic cloning**”.

Therapeutic cloning is therefore a method by which 100 percent immune compatible embryonic stem cells can be generated from a human being in need of therapy. Therapeutic cloning differs from reproductive cloning in the fact that pre-implantation embryos generated in the laboratory will never be transferred from a petri dish into the uterus.

In general, the procedure of therapeutic cloning involves the superovulation of volunteer women and the harvesting of mature eggs. The eggs are then transported to the laboratory where the DNA is removed thereby creating an enucleated egg. A patient donates cells from his or her skin which are then fused with the enucleated human egg. The chromosomes are removed from the egg and put in the new DNA from the patient.

After about five or six days, in vitro human embryos will reach a stage that is called the blastocyst stage. It is at this point that the subset of cells is removed and placed in a petri dish, allowing the embryonic stem cells to grow indefinitely. The modification of the culture conditions will induce cells to grow into specific cell types to be reintroduced into the patient.

Stem cells derived from surplus IVF embryos and used for transplantation could have problems with genetic or immune rejection of those cells. If they were derived from unknown eggs, they would not match the person you want to give the cells to, and they could be rejected.

It has been proposed that cloning technology could be used to generate stem cells that would match the person you want to give the graft to thereby avoiding the rejection problem. **That is why people talk about cloning in connection with stem cells and why it is so urgent for policy makers to deal with cloning in legislation.**

QUOTABLE QUOTES

Of particular concern is a potential abuse of in vitro fertilization as a backdoor way of dealing with a growing need for stem cells. This would injure the sound principles upon which are based the proposal for assisted human reproduction. (Testimony before the Standing Committee on Health)

**Mr. Yves Savoie, Executive Director,
Muscular Dystrophy Association of Canada**

Embryonic stem cells have a limited life span in culture. They're technically immortal, but what happens is that they accumulate mutations, and there is a genetic drift in that population. Fresh embryonic stem cells behave very differently from old stocks. (Testimony before the Standing Committee on Health)

**Dr. Michael Rudnicki,
Ottawa Health Research Institute**

While adult stem cells may never be as completely “plastic” as embryo stem cells, they will almost certainly be plastic enough for all practical applications. These adult stem cells don't appear to be as restricted in their fate as we thought they were.

**Professor Dennis Steindler,
University of Tennessee-Memphis, May 2001**

The merging truth in the lab is that pluripotent embryonic stem cells are hard to rein in. The potential that they would explode into a cancerous mass after a stem cell transplant might turn out to be the Pandora's box of stem cell research.

**Dr. Glen McGee, Bioethicist,
University of Pennsylvania, May 2001**

Chapter 3

ADVANCES IN RESEARCH

Today around the world, literally hundreds of millions of people suffer from debilitating diseases which have impaired their quality of life in innumerable ways.

Just think of the number of different agencies that work so tirelessly year after year to raise funds for research in the hope that an elusive cure can be found. Cancer, heart and stroke, Alzheimer's, Parkinson's, muscular dystrophy, diabetes, blindness, spinal cord injury, muscular sclerosis are but a few that come to mind.

It is not difficult to understand why so much hype can be generated by research developments which offer a glimmer of hope. Any step closer to cure has enormous implications both to those who hold out hope and those who can deliver research progress.

A big part of delivering research progress will come as a result of the **Human Genome Program**. The human genome has been described as the blueprint from which humans are derived. Knowledge of this blueprint is widely touted as the first step towards the prevention, diagnosis, and treatment of disease as well as its cure.

Begun in 1990, the U.S. human genome project is a 13 year effort coordinated by the Department of Energy and the U.S. National Institutes of Health. The project was originally planned to last 15

years, but effective resource utilization and technological advances have accelerated the expected completion date to 2003. The project goals are:

- To identify all the approximately 30,000 genes in human DNA
- To determine the sequence of the 3 billion chemical base pairs that make up human DNA
- To store this information in databases
- To improve tools for data analysis
- To transfer related technologies to the private sector
- To address the ethical, legal, and social issues that may arise from the project

Several types of genome maps have already been completed and a working draft of the entire human genome sequence was announced on June 26, 2000, by President Bill Clinton and British Prime Minister Tony Blair.

Many diseases involve irreversible degeneration of some crucial cell type or tissue: islet cells of the pancreas in diabetes, neurons of the brain in Parkinson's disease, Huntington's disease and other neurological conditions.

Researchers have worked for years to discover ways of developing human cells in laboratory culture that could regenerate failing tissue but they have had serious challenges to overcome. For example cancer cells grow readily in a bottle but healthy, normal ones soon stop propagating outside the body. This was overcome with the discovery of stem cells.

Scientists were able to identify and culture, for many months, rare stem cells from various critical tissues. The cells, when implanted in the appropriate type of tissue, could regenerate the range of cells normally found there.

Stem cells have been discovered in the nervous system, muscle, cartilage and bone and probably exist in pancreatic islet cells in the liver. Research work also found special cells derived originally from a fetus could produce a wide variety of tissue-specific cells.

In 1991, Irving Weissman of Stanford University discovered a type of human stem cell found in bone marrow which gives rise to a full range of cells in blood. The importance here is that a cancer patient whose marrow has been destroyed by high doses of radiation or chemotherapy can be saved by transplant of cells derived from bone marrow.

Researchers have also learned that stem cells exist in tissues such as the brain where they can give rise to all three of the common cell types found there. They found that central nervous system stem cells grown in the laboratory can engraft in mouse brains and alleviate behavioural abnormalities in animals which were genetically engineered to mimic the features of Parkinson's disease.

Although they may constitute only one in every few thousand tissue cells, stem cells can be isolated by specific molecules they display on their surfaces. One way to make use of stem cells would be to extract them from a tissue sample given by a patient or donor and then multiply them in the laboratory. Growing tissue specific stem cells from donors or patients does, however, have a disadvantage. With each division, the structures at the end of the chromosomes, known as "telomeres", shorten slightly causing the

reengrafting cells to age prematurely and possibly limit their growth potential.

This seems to have been the case with **Dolly, the cloned sheep**, who has prematurely developed arthritis in one of her legs. To address this problem, researchers are turning to other tissue-specific stem cells from a different source.

These non-aging cells are called embryonic germ cells. These ultimately versatile cells can be cultured indefinitely and give rise to every cell type found in the body. They are similar to what in animals are called embryonic stem cells.

In addition, researchers are working with an enzyme called **telomerase** which seems to prevent the telomeres at the ends of chromosomes from getting shorter each time the cell divides. Several researchers have also now shown that animal embryonic stem cells can be induced to develop into tissue specific cells by bioengineering techniques.

Isolating and culturing stem cells is still an exacting task. Stringent safety testing is needed before physicians could introduce modified cells into a patient because they could conceivably become cancerous.

However, the long-term potential is considered to be very strong and research aggressively continues to utilize human stem cells in their drug development efforts.

It was long thought that the human body builds up most of the cells and tissues early in life and that everything begins to fall apart, cell by cell. Actually this is not the case. **Stem cells are working away throughout our lives fixing problems and repairing damage to cells and tissue.**

For example, the stem cells located in bone marrow must replace more than 1 billion red blood cells every day. This kind of rebuilding is going on constantly all over the body. Stem cells also make new cells continuously for bone, liver, heart, muscle and even the brain where we once thought there was no possibility of generating new cells.

Stem cells also serve as a natural defence against aging. As things wear down, the cells work to repair some damage. However, as we get older, the failures in our bodies apparently overrun the stem cells. Consequently, we get slower, weaker and more forgetful. Scientists believe that one day we might even be able to fight off this degeneration and keep us living longer and healthier lives with a regular dose of stem cells.

In late 1998, researchers at Johns Hopkins University and the University of Wisconsin-Madison isolated human stem cells for the first time. This was a major breakthrough which raised hope for therapeutic uses of stem cells as well as a range of ethical questions.

With stem cells now being readily available, scientists launched a variety of animal experiments. At the Harvard Medical School, scientists showed that neural stem cells seek out damaged areas of the mouse's cortex and make new neurons there.

There is also preliminary evidence that neural stem cells can do this in primates as well and that neural stem cells could generate new neurons in other areas of the brain and even in the spinal cord. **If human neural stem cells can go to damaged areas in the nervous system and create neurons there, this just might be the cure or defence against Parkinson's disease, Lou Gehrig's disease or old-age dementia.**

In July, 2001, The New England Journal of Medicine reported that surgeons in Taiwan restored vision to patients with severe eye damage by using stem cells from the patient's own eyes.

As well, the journal Nature reported that British scientists found that adult stem cells in bone marrow can turn into liver tissue, a first step towards developing new treatments for liver damage.

At the University of Florida, their findings showed that a cell that originated in the bone marrow of a rat could travel to the liver and become a functioning liver cell. Presumably, that bone marrow cell was initially a blood making stem cell.

This was some of the first evidence that stem cells that have been defined in different tissues are actually capable of hopping from one tissue to another. This means the cells are capable of giving rise to cells of another tissue such as brain to blood, brain to muscle, pancreas to liver, muscle into blood.

The question scientists are still working on is whether the transformed cells are working properly. Just because it looks like a new cell doesn't mean that it works properly.

The controversy around stem cells revolves around the issue of destroying embryos. There are two general sources of stem cells, ones that come from embryos (or aborted fetus') and ones that come from a variety of adult tissues which occur naturally in the body.

One would think that if you can get stem cells from adult tissues, there is no need to get into an ethical controversy by using embryos. Scientists have found that embryonic stem cells have the potential to form any cell in the human body and this is why they are referred to as being pluripotent.

The one problem with embryonic stem cells is that they are not genetically compatible with the recipient patient and therefore are subject to rejection by the immune system. It is not clear what the developmental potential is of adult stem cells, but research developments have shown that adult stem cells are much more versatile than originally thought.

Unlike the situation with embryonic stem cells, adult stem cells taken from the patient would be genetically compatible and therefore not subject to the risk of rejection. As science learns more about stem cells and how they operate, technology may be able to induce adult stem cells to do virtually every task.

There is also some concern that adult stem cells may be partially worn out so that they could not offer the full rejuvenating benefits of embryonic stem cells. This is also the subject of current research activity.

Due to funding restrictions, most of the early research was confined to a few private biotechnology companies such as **Geron Corp. and Advanced Cell Technologies Inc. (ACT)**.

The technique being developed by ACT was called nuclear transfer in which researchers removed the nucleus from a cow's egg, implanted a human cell and allowed it to grow embryonic stem cells. The human cell would come from skin cells such as those on the inside of your cheek which would make embryonic stem cells just for that person.

That could be important because the immune system might fight off stem cells from anyone else, seeing them as foreign invaders like a virus. The immune system searches out foreign cells very efficiently and destroys them. According to ACT, they can grow

these cells in culture and keep them alive essentially forever. Their testing kept the cells growing for well over one year.

Once researchers know how to culture a certain kind of cell, they can make incredibly large numbers of them. For example, **a single human skin cell can spawn 170 trillion trillion trillion cells.** This means that forming the cells in culture could reduce the concerns of using embryonic tissue.

ACT has created the not-for-profit WiCell Research Institute to grow and sell human embryonic stem cells for research. They estimate that clinical trials with human neural stem cells could take place within a couple of years. That means that stem cell treatments could be available for clinical applications in 5 to 10 years.

In early 2001, ACT launched its attempt to create a cloned human embryo. They began by consulting with their Ethics Advisory Board and received the go-ahead. Next they recruited women willing to contribute eggs to be used in the cloning procedure and also to collect cells from individuals to be cloned.

In the basic nuclear transfer technique, scientists use an extremely fine needle to suck the genetic material (DNA) from an immature egg. They then inject a nucleus of the donor cell into the enucleated egg before treating it to a chemical bath and electrical stimulation. This reprogrammed the body cell's DNA back to an embryonic state in which it will divide and grow stem cells identical to the patient's.

They accepted women only between the ages of 24 and 32 who had at least one child. Potential contributors also submitted to psychological and physical tests including screening for infectious diseases to insure that the women were healthy and that

contributing eggs would not adversely affect them. Skin biopsies were taken from several anonymous individuals to isolate cells called fibroblasts for use in the cloning procedure.

The first cloning attempt occurred in July 2001 and on October 13, 2001, they generated their first cloned human embryo. **It took a total of 71 eggs from seven volunteers.** In the final test, two eggs divided to form early embryos of four cells and one progressed to at least six cells before growth stopped.

ACT also wanted to determine whether they could induce human eggs to divide into early embryos without being fertilized by a sperm or being enucleated and injected with a donor cell. Although mature eggs and sperm normally have only half the genetic material of a typical body cell (to prevent an embryo from having a double set of genes following conception) eggs halve their genetic complement relatively late in their maturation cycle. If activated before that stage, they still retain a full set of genes.

This process is called “**parthenogenesis.**” Stem cells derived from such parthenogenetically activated cells would be unlikely to be rejected after transplantation because they would be very similar to a patient’s own cells and would not produce any molecules that would be unfamiliar to the person’s immune system.

It is hoped that such cells might also raise fewer moral dilemmas for some people than would stem cells derived from cloned early embryos. In their experiments, ACT exposed 22 eggs to chemicals that changed the concentration of charged atoms called ions inside the cells. After five days of growing in culture dishes, six eggs had developed into what appeared to be blastocysts but none clearly contained the so-called inner cell mass that yields stem cells.

On November 25, 2001, ACT publicly announced that it had cloned its first human embryo and it met with swift condemnation from around the world. A statement from the Vatican said, “notwithstanding the humanistic intents ... this calls for a calm but resolute appraisal which shows the moral gravity of this project and calls for unequivocal condemnation. What we have before us are human embryos and not cells ... life which must preserve its dignity like every other human life.”

President Bush also criticized the experiment, saying, “We should not as a society grow life to destroy it and that is exactly what’s taking place.”

There is no question that cloning crosses everyone’s moral line in the sand regardless of how beneficial it might be in treating diseases.

QUOTABLE QUOTES

Human embryos obtained in vitro are human beings and are subjects with rights; their dignity and right to life must be respected from the first moment of their existence. It is immoral to produce human embryos destined to be exploited as disposable biological material.

Pope John Paul II, 1995 encyclical “The Gospel of Life”

The biomedical potential of embryonic stem cells remains entirely speculative because such cells have never been used successfully in clinical applications. They also present the possibility of tissue rejection, which would require drug therapy for life, and tumour growth.

Dr. John Shea,

Fellow of the Royal College of Physicians of Canada

In a biological bakery, embryonic stem cells can be considered the flour. Add some ingredients and the flour is converted into a cake, while other ingredients produce bread or biscuits or even gravy. It all depends on what is added to the flour and how the dough is processed.

Paul Recer, Columnist, Associated Press, August 10, 2001

Another advantage of adult stem cells might be considered from a manufacturing viewpoint: A 2-step manufacturing process is more direct and has much less likelihood of a problem than a 10-step process (of embryonic stem cells). Injected into the body, embryonic stem cells can produce tumours. No such problems exist with adult stem cells.

David Prentice, Professor of Life Sciences,

Indiana State University, February 26, 2001

Chapter 4

ETHICS AND MORALS

The cloning of Dolly the sheep and the mystery of the Human Genome Project capture the imagination, but the potential magic of stem cells has seized the public interest like no other scientific development.

We were moved by stories about Christopher Reeves, alias Superman, who had suffered a debilitating spinal cord injury, trying to convince U.S. politicians that stem cells could be the key to repairing spinal cord injuries. Similarly Michael J. Fox had made his case about the promise of stem cells in curing his Parkinson's disease or Mary Tyler Moore and her diabetes. There was no question that stem cells were now viewed as the universal cure for all that ails us and that we should do everything possible to move that research forward.

You cannot pick up a newspaper or magazine without reading another story about the promise, the hope and the potential of stem cells. The hype is enormous and one would think treatments are already available. **In fact, clinical trials on humans have not even started but rather all the scientific data is based on work on mice, rats and primates.**

Some human trials may start within a couple of years and it is estimated that the actual treatments may not be available for 5 or 10 years. The reason why it will take so long is that the science really hasn't been perfected and we really don't know whether

stem cell therapy is safe and will not have unintended consequences.

Human beings are tremendously complex and diverse organisms and what might work for one person may also have horrific consequences for another. **When you tinker with Mother Nature, almost anything can happen and that is why ethical considerations become so relevant to stem cell research.**

No new scientific or technological development can claim immunity from ethical scrutiny. The fact that new technologies exist does not necessarily mean that they ought to be employed. Our moral views also have considerable practical importance in informing and influencing public attitudes, choices and behaviours. In short, they help to shape our view of the world.

Some years ago, I served on the Ethics Committee of the Board of Directors of the Mississauga Hospital. Although I had no formal education in ethics, we attended seminars and were provided with briefing books and reference material to make us aware of the important ethical principles and practices which should guide our decisions. We also had the assistance of a professional ethicist to help us work through issues where science, ethics, law and human rights were not in harmony.

We reviewed hospital policy and case studies and we monitored ethical standards and practices to ensure that the medical staff had the support and guidance they needed in making life and death decisions on a daily basis.

Medical ethics or bioethics is the study of moral issues in the fields of medical treatment and research. The term is also sometimes used more generally to describe ethical issues in the life sciences

and the distribution of scarce medical resources. The professional fields that deal with ethical issues in medicine include medicine, nursing, law, sociology, philosophy, and theology.

Medical ethics traces its roots to several early codes of ethics such as the ancient Greek Hippocratic Oath, which required physicians above all to “do no harm”; professional codes of ethics such as the one written by English physician Thomas Percival in the 18th-century that provided the foundation for the first code of ethics established in 1846 by the founders of the American Medical Association; and the Nuremberg Code for research ethics on human subjects that was established during the war crime trials at the close of World War II (1939-1945) in response to the gross abuses in human experimentation performed in Nazi Germany.

The advent of new medical and reproductive technologies after the 1950’s further complicated the moral and societal issues of medical research and practice.

The Natural Sciences and Engineering Research Council of Canada has a very good paper on its Web site which describes a basic ethical framework. The elements of this framework include establishing the need for research, moral imperatives, ethical principles and the law.

Research involving human subjects is premised on a fundamental moral commitment to advancing human welfare, knowledge and understanding. The three general categories of benefits are the basic desire for new knowledge and understanding; the quest to advance knowledge; and research that benefits particular groups and society as a whole.

An ethic of research involving human subjects should include two essential components. First is the selection and achievement of

morally acceptable ends and secondly, the morally acceptable means to those ends.

Guiding ethical principles have evolved over decades and have been widely adopted by diverse research disciplines. As such they express common standards, values and aspirations of the research community and include the following:

- **Respect for Human Dignity:** This principle aspires to protecting the multiple and interdependent interests of the person from bodily to psychological to cultural integrity.
- **Respect for Free and Informed Consent:** Individuals are presumed to have the capacity and right to make free and informed decisions.
- **Respect for Vulnerable Persons:** This entails high ethical obligations towards vulnerable persons such as those with diminished competence, children and institutionalized persons.
- **Respect for Privacy and Confidentiality:** Respect for human dignity also implies the principles of respect for privacy and confidentiality.
- **Respect for Justice and Inclusiveness:** Justice connotes fairness and equity.
- **Balancing Harms and Benefits:** The analysis, balance and distribution of harms and benefits are critical to the ethics of human research. Foreseeable harms should not outweigh the anticipated benefits.

- **Minimizing Harm:** A principle directly related to harms-benefits analysis is non-maleficence or the duty to avoid, prevent or minimize harms to others.
- **Maximizing Benefit:** Another principle related to the harms and benefits of research is beneficence. The principle of beneficence imposes a duty to benefit others and, in research ethics, a duty to maximize net benefits.

The law affects and regulates the standards and conduct of research involving human subjects in a variety of ways, such as privacy, confidentiality, intellectual property, competence, and in many other areas. Human rights legislation prohibits discrimination on a variety of grounds. In addition, most documents on research ethics prohibit discrimination and recognize equal treatment as fundamental.

Research ethics boards should also respect the spirit of the Canadian Charter of Rights and Freedoms, particularly the sections dealing with life, liberty and the security of the person as well as those involving the quality of life and discrimination.

The Hippocratic maxim “do no harm” has long been a fundamental principle of medical ethics. One should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful. Further, we need to determine when it is justifiable to seek certain benefits despite the risks involved and when benefits should be foregone because of the risks.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development

are benefits that serve to justify research involving children - even when individual research subjects are not the direct beneficiaries.

Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, with research that presents more than minimal risk without immediate prospect of direct benefits to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. As with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

Ill health and death are a part of life and sometimes we have to let nature take its course. If you ever wanted to have an endless discussion, just start debating whether life support is extending life or prolonging death or what do we mean by quality of life or when you should not try to resuscitate a patient in cardiac arrest. What do we mean by informed consent? Who can override a no CPR order? What do we mean by mental competence? Do I have the right to die? Do I have the right to live? Do I have the right to the best possible care or is it restricted to the best possible care available and affordable? Do I have a right to sell my organs? Can I deny treatment? Do I have the right to know everything about my medical condition? Can a medical professional withhold any information?

These are but a few of the questions that were addressed by the hospital Ethics Committee and most of the discussion involved the principles of ethics. However, from time to time, what was right

and what was wrong became a big part of the decision making process. The morality of an issue was often as important as the ethical considerations.

The book “Improving Nature?” by Michael Reiss and Roger Straughan offers a concise perspective on the connection between morals and ethics. Their first observation is that the terms “moral” and “ethical” are often used without definition, implying that their meanings are self-evident and synonymous.

The difference is subtle but important to bringing clarity to the arguments about the validity of moral and ethical concerns. **Everyone can be said to have moral views, beliefs or concerns about what is right and wrong and what ought or ought not to be done.** These views can refer to virtually any subject and relate to the subject itself or the consequences flowing from the subject. Some moral concerns come from deliberation and reflection or be grounded in rational principles or be consciously analysed. They can also come from our upbringing or simply from intuition. As such, moral views are personal and dynamic.

Ethics on the other hand is a narrower concept than morality. It may refer to a set of standards set by a group or community to regulate behaviour such as in business or medical ethics. More technically, ethics can also refer to a particular branch of philosophy. In this sense, ethics is usually taken to be a critical investigation of the fundamental principles and concepts that are used in moral debate.

Ethics tries to analyze and clarify the arguments that are used when moral questions are discussed, and to probe the justifications that are offered for moral claims. In effect, ethics scrutinizes our moral beliefs. Therefore the existence of a moral concern does not necessarily mean there is an ethical concern. For example in the

case of genetically modified foods, many have moral concerns because GMOs were unnatural or even frightening but there is apparently no ethical breach by producers.

It is a natural reaction to have the fear of the unknown. Without proof to the contrary, we can see risk or even catastrophe because you can always find an example in history. Take the example of the fertility drug thalidomide. It was supposed to help a woman to conceive a child and despite all the testing that was done, a generation of limbless children was born.

Safety is an extremely important prerequisite and that is why whenever we interfere with or modify nature, red flags go up. Unnatural transplantation, cross-pollination, genetic modification, artificial stimulants, chemicals and pharmaceuticals all require the burden of proof of safety.

When it comes to new products, new techniques, new technology or just new and improved, we want to know the justification for the need. We want to know who is responsible. We want to know who is accountable. We want to know whether a proper assessment of the risks has been made. We want to know what benefits should be expected. We want to know what it will cost. We want to know whether performance is guaranteed. We are a demanding society that seeks a 100% confidence level when it comes to matters of our health and well-being.

Extreme caution can cause paralysis whereas uncontrolled experimentation can lead to irresponsibility. As well, it is difficult for ethical judgment to be made about issues of risk and safety. For that reason, opposing views always seem to hold out for the compromise of justifiable risks. Safety can never be totally proved and therefore judgment has to be made about the likelihood

of possible consequences and the relative value, desirability and priority to be assigned to these. This is an area where **it is essential that science and ethics proceed hand-in-hand.**

In our society, we also have some biases when it comes to what is natural and what is unnatural. Natural has become a synonym for good or better or real. Unnatural on the other hand has become a synonym for bad or unhealthy or artificial.

However, many natural substances are harmful and many of our natural tendencies such as jealousy and aggression are not normally thought of as morally praiseworthy. Nevertheless, we are judgmental by nature and we will use words interchangeably if it suits our purpose, a behaviour which, in itself, may be unethical but which is not immoral.

Scientists from Canada, the United States, Britain, Japan, Germany and France had been working on the Human Genome Project since the early 1980s and in February 2001, the first complete set of human genetic instructions was published by Celera Genomics Corp. It was a 3 billion letter sequence that spells out the genetic code for a human being. Even though they didn't understand it, the public was fascinated by the concept of the human genome and DNA. There was no reaction from the standpoint of morality or ethics. However, gene research and particularly cloning quickly raised concern about complex ethical issues.

The most contentious ethical issue arising from stem cell research is the derivation of embryonic stem cells. Some believe that the human embryo is a being with full moral status from the moment of conception and has an inalienable right to life. Others consider that an early human embryo is just a collection of cells and that its moral status is equivalent to that of any other cells in the body.

The fundamental question to be answered is “When does human life begin?” The position of the CIHR is expressed in the *Tri-Council Policy Statement*. It is a graduated approach whereby the human embryo has a specific moral status as a *potential person*. In this view, the human embryo has neither the full moral status of a person nor an absolute right to life.

However, in 1995, the highly respected Ramsey Colloquium statement on embryo research opines that: “The embryo is human; it will not articulate itself into some other kind of animal. **Any being that is human is a human being.** If it is objected that, at five days or fifteen days, the embryo does not look like a human being, it must be pointed out that this is precisely what a human being looks like - and what each of us look like - at five or fifteen days of development.”

In addition, the Center for Bioethics and Human Dignity reported that “an international scientific consensus now recognizes that human embryos are biologically human beings beginning at fertilization, and acknowledges the physical continuity of human growth and development from the one cell stage forward.”

Notwithstanding the position of the CIHR, an international scientific consensus recognizes that human embryos are human beings from conception. Although some researchers may consider the human embryo to be mere biological tissues or clusters of cells, **it is an objective biological fact that embryos are human beings.**

The moral and ethical arguments also need to be considered in the context of the cloning debate. Cloning is carried out by a process known as “cell nuclear replacement.” The nucleus of a human egg

is removed and replaced with the nucleus from a cell of the person from whom the clone is to be produced. The cell is then artificially stimulated and begins to develop into an embryo in the same way that a fertilized egg develops. **The reality is that both reproductive and therapeutic cloning involve the creation of new human beings**, who, being very small and at an early stage of development, should be accorded the extra special protection of law.

The only difference between therapeutic and reproductive cloning is that, in the former, the human embryo is broken up at an early stage known as the blastocyst stage. At this stage, the cells are undifferentiated but thereafter if they are allowed to develop, the cells in the blastocyst will begin to develop into different organs and tissue.

What scientists wish to do is to take the stem cells from a blastocyst to see if they can encourage these individual cells to grow into particular types of tissue which might possibly be used to replace or repair tissue in an older patient. Some think, that in many respects, therapeutic cloning is even more barbarous than reproductive cloning since it involves the tearing to pieces of a specially created human embryo.

What is being advocated, therefore, is the use of specially created, cloned embryos as sources of stem cells for the treatment of various medical conditions even though such cells can also be harvested without destruction of embryos from umbilical cord blood, bone marrow, blood or other adult stem cells.

The presumption by all who support embryonic stem cell research is that this scientific activity will in fact produce some positive medical benefits. Very little has been written about the failure rates

of experimentation or in fact the horrendous results that often occur. The New England Journal of Medicine recently published a report on a carefully controlled study that tried to treat Parkinson's disease by implementing cells from aborted fetuses into patients' brains.

Not only did the tests fail to show an overall benefit but also revealed the **disastrous side effect in 15 percent of the patients**. The implantations produced uncontrollable movement (writhing, twisting, jerking) and there was no way to deactivate or remove the transplanted cells. Dr. Paul Greene, a neurologist at Columbia University's College of Physicians and Surgeons said, "It was tragic, catastrophic, a real nightmare and we can't turn it off."

The desire to heal people is certainly a laudable goal but many ethicists have reminded us that **it is not ethical to pursue good ends by unethical means**. The destruction of some human beings for the benefit of other human beings is simply wrong. It is an affront to human dignity; it is not the only means of achieving the proponent's purposes; it is not well enough understood to be trusted as a curative mechanism; it appears to carry with it the most dangerous and irreversible side effects; and may not have any significant curative properties. For these reasons, many oppose research using stem cells obtained by destroying human embryos.

Given all the facts, even the general public agrees according to recent polling. Between June 1st and June 5th, 2001, International Communications Research, a national polling firm headquartered in Pennsylvania, carried out a poll of one thousand American adults. The two questions and the results are as follows:

1. Stem cells are the basic cells from which all of a person's tissues and organs develop. Congress is considering

whether to provide federal funding for experiments using stem cells from human embryos. The live embryos would be destroyed in their first week of development to obtain the cells. Do you support or oppose using your federal tax dollars for such experiments? (23.9% Support, 69.9% Oppose, 4.8% Don't know, 1.3% Refused to answer)

2. Stem cells for research can be obtained by destroying human embryos. They can also be obtained from adults, from placentas left over from live births, and in other ways that do no harm to the donor. Scientists disagree on which source may end up being the most successful in treating diseases. How would you prefer your tax dollars to be used this year for stem cell research? (17.6% supported all methods, 66.8% supported research using adult stem cells and other alternatives, 8.6% supported neither, 6.3% don't know and 0.7% refused to answer)

The results seem to be consistent. In each case, destruction of human embryos was not supported by a clear majority. With the knowledge that there was an alternative to destroying human embryos, the support for destroying human embryos dropped even further.

Health Canada also commissioned a poll by the polling firm Pollara on attitudes towards embryonic stem cell research which would be used to tailor draft legislation on the issue. The poll asked respondents, "In your opinion, should allowing research on human embryos be banned, regulated or remain as it is?" The poll showed 71% of Canadians would allow research on human embryos, 26% would ban such research and 3% would leave it as is. The polling firm did not inform the respondents that when human embryos are used for stem cell research, they would be destroyed. It also did not mention that there were equally

promising ethical alternatives which do not involve destruction of human embryos.

The Canadian results are exactly the opposite of the U.S. poll results. Is it possible that the attitudes of Canadians are so much different from our U.S. neighbours? The CIHR does not consider the human embryo as a human being at conception and believes that adult stem cells are inferior to embryonic stem cells. Health Canada has proposed draft Canadian legislation built on those views.

Dr. Thomas P. Dooley is the CEO of IntegriDerm Inc., CEO of ALtruis LLC, and President of the Biotechnology Association of Alabama. One might think that someone with such a strong vested interest in the biomedical research industry would be an aggressive advocate for embryonic stem cell research. However, in July 2001, he wrote an article entitled, “The Dilemma Of Embryonic Stem Cell Research”, which lays out his serious concerns and recommendations.

Dr. Dooley expresses a concern that the scientific community has not objectively assessed the alternatives nor have the general public given any serious thought to the broad consequences of embryonic stem cell research. He suggests that the most important reason to give consideration to this issue at this critical time is the ethical, moral, and religious “can of worms” that it opens up. He goes on to say that any research on embryonic stem cells is work performed on the early stages of life of a human being.

Although some proponents of embryonic stem cell research might carefully “wordsmith” their arguments to make this issue less clear and more palatable to the unaware, it is biologically true that the entire potential for a human being

rests in the zygote (fertilized egg). A human being starts biologically as a zygote. Therefore, he suggests that any research performed on the zygote or early embryo has the potential and is very likely to terminate a human life, just like therapeutic abortions.

He argues that research on embryonic stem cells replaces the potential of a human being for the potential of the desired research outcome. It is literally that simple. Does one discard one option for the other? It is arguably difficult to advocate for embryonic stem cells, if an individual is ethically, morally or religiously opposed to this research methodology. He believes that the dilemma is also compounded by the fact that the scientific justifications and merits of embryonic stem cell research have not yet been demonstrated.

For these reasons, he makes the following recommendations:

1. We must educate the public regarding the differences between embryonic and adult stem cell research with regard to the science and the ethical dimensions.
2. We should ban research of any kind involving human embryonic stem cells.
3. We should ban the intentional creation of human life by means of cloning or use of embryonic stem cells.
4. We should ban the intentional creation of human life in which the zygote has been genetically modified by any means.
5. Funding should be banned on research for items 2, 3 and 4 above.

6. We must hold accountable researchers and clinicians who violate imposed restrictions.
7. We should proceed cautiously with research proposals involving adult stem cells.

In another article entitled, “No Imperative To Clone Human Beings”, Dr. Dooley gave his commentary on the recently announced cloning of a human embryo by Advanced Cell Technologies Inc. In his view, at an experimental level this was not a big deal but at a moral level it was a huge deal. He had expressed concern for some time about the fast approaching highly unethical practices such as human cloning.

He is worried that without compelling restraint, scientists and physicians are moving forward rapidly to develop human cloning methodologies that could be used for reproductive cloning or therapeutic cloning which would intentionally destroy the newly created embryonic cells for other research projects. The same methods can be used for either desired outcome.

While he is a strong advocate for funding of biomedical research, he believes that some research should not be conducted if credible moral objections can be raised. He believes in spending money on research that raises little or no objections from society. He suggests that in their haste to move forward, the whole truth is being overlooked or suppressed by advocates of therapeutic cloning. He notes that outstanding advances in research and medicine are created using pharmaceuticals, biotechnology products, surgical methods, and adult stem cells. As such, he believes that human cloning is unnecessary.

Dr. Dooley also raises **the issue of profit motive**. He states that some companies and academic researchers are moving forward with human cloning methods simply because of the money. In his experience, if the money trail dried up for human cloning research, well-trained scientists would simply work on something else.

He also identifies that one of the central issues of this dilemma focuses upon the definition of a human being. He believes that human beings are created with special attributes entitling them to treatment with dignity and rights. He suggests, however, that advocates for human cloning view small human beings at early stages of life to be mere commodities.

He suggests that we pose the following two questions to advocates of human cloning:

1. Do we realize that human lives are being terminated in these experiments for the sake of the potential of a subsequent research experiment?
2. Are early stage embryos really human beings entitled to dignity and rights?

In his view, their answer to both questions would be a loud “No”. He argues that if they are presumed to be correct, then what is the difference between a one week-old human embryo or a nine month old baby the day prior to birth or a 72 year-old grandmother? When do dignity and rights begin, if not at the start of life?

QUOTABLE QUOTES

There must be a higher notion than science alone that can guide scientific research and endeavour. Simply because we can do something does not mean that we should do it.

The Hon. Allan Rock, Minister of Health, May 3, 2001

Unless and until we are confident that we should proceed with the novel and ethically controversial activities identified, it is imperative that they be prohibited. The first thing to recognize in the legislation and in all of your conversations is that embryos are human beings. That is an uncontested biological fact. They are a member of the human species.

**Ms. Francoise Baylis, Associate Professor,
Department of Bioethics, Dalhousie Medical School**

The Commission found that the evidence shows that there's a real possibility the use of fetal tissue transplant could result in considerable alleviation of human suffering in some devastating disorders. If you were to prohibit pursuit of such research, I think it would be uncaring and unethical. (Testimony before the Standing Committee on Health)

**Dr. Patricia Baird, Chair of The Royal Commission On
Reproductive and Genetic Technologies (1989-1993)**

In a way, the stem cell of all stem cells is the fertilized egg, a zygote having a unique 46-chromosome endowment, half of which is contributed by a genetic father and half by a mother. This is an utterly unique cell, endowed with all the information that marks the launching of an individual career. If any of the other 100 million or so sperm present in the act of intercourse had penetrated the ovum, it would not have become you, but someone else.

Author John F. Kavanagh, June 3, 2000

Chapter 5

THE GREAT U.S. COMPROMISE

In 1994, a Federal panel, established by the National Institutes of Health, to examine the scientific, legal and moral issues surrounding the use of human embryos and research, tabled its report. One of its recommendations was that researchers ought to be allowed to create human embryos for research purposes.

As the recommendation was met with public outcry, President Clinton issued an executive order prohibiting the use of federal funds to create embryos for research. The president's executive order has been followed by a number of congressional bans on federal funding for human embryo research that have been attached to NIH funding legislation.

On September 7, 1999, the U.S. National Bioethics Advisory Commission sent its report, "Ethical Issues in Stem Cell Research", to President Clinton. Before the report was finished, it had already become a source of controversy. The key point of controversy was the commission's recommendation to use human embryos, originally intended to be used for infertility treatments but now no longer needed, as a source for stem cell research.

On August 23, 2000, the Clinton administration released a set of parameters guiding the use of specific embryonic cells, called stem cells, for federally funded medical research. In general the rules laid out that embryonic cells must be harvested by privately funded labs and passed on to the federally funded scientists, in order to avoid having government monies directly linked to the destruction

of an embryo. Researchers were also restricted to use only embryos that were marked to be discarded and embryo donors were not to be reimbursed.

If the guidelines made it through Congress, they were to apply to grant applications submitted after January 2001 which was very strategic. By that time, a new President of the United States will have been sworn in and the guidelines would need Presidential approval prior to coming into effect.

Governor George W. Bush publicly opposed federal funding for stem cell research that involves destroying a living human embryo. **Violent opposition had already surfaced in both the House and the Senate and it was evident that the battle lines were forming throughout the country.**

On January 4th, 2001, even before George Bush took office, his Press Secretary, Ari Fleischer commented that the new administration would probably axe public funding of medical research using stem cells and that is exactly what happened. Bush did ask federal researchers for more information on the issue and on July 17, 2001, the confidential report from the National Institutes of Health was delivered.

It was also formally presented to a Senate Subcommittee the following day. It included the most up to date information available but made no recommendation one way or the other on federal funding. Both sides contended that the report validated their arguments but the most consistent theme in the report was that more research was needed before any firm, scientific conclusion could be reached on the relative medical value of stem cell types.

Hearings on stem cell research had been going on since April 2000 and no view was left unrepresented. The President was also lobbied heavily from all sides in anticipation of a new policy. Rumours started to surface that Bush was prepared to fund stem cell research. With everyone waiting to hear a “yes” or a “no”, Bush took many by surprise with a policy position that drew criticism from many directions and from both sides.

Bush was only deciding whether there would be federal funding for stem cell research unlike Canada’s proposed approach to permit such research under certain conditions. Regardless of his decision, private laboratories would not be affected in their work because they relied on private funds.

Notwithstanding, the rationale for his decision, the reasons are substantively the same as they would have been had he been deciding whether to ban embryonic stem cell research all together. The following is a transcript of President George Bush’s speech on August 9, 2001, in which he announced his long-awaited decision to the nation:

Good evening. I appreciate you giving me a few minutes of your time tonight so I can discuss with you a complex and difficult issue, an issue that is one of the most profound of our time.

The issue of research involving stem cells derived from human embryos is increasingly the subject of a national debate and dinner table discussions. The issue is confronted every day in laboratories as scientists ponder the ethical ramifications of their work. It is agonized over by parents and many couples as they try to have children, or to save children already born.

The issue is debated within the church, with people of different faiths, even many of the same faith coming to different conclusions.

Many people are finding that the more they know about stem cell research, the less certain they are about the right ethical and moral conclusions.

My administration must decide whether to allow federal funds, your tax dollars, to be used for scientific research on stem cells derived from human embryos.

A large number of these embryos already exist. They are the product of a process called in vitro fertilization, which helps so many couples conceive children. When doctors match sperm and egg to create life outside the womb, they usually produce more embryos than are planted in the mother. Once a couple successfully has children, or if they are unsuccessful, the additional embryos remain frozen in laboratories. Some will not survive during long storage; others are destroyed. A number have been donated to science and used to create privately funded stem cell lines. And a few have been implanted in an adoptive mother and born, and are today healthy children.

Based on preliminary work that has been privately funded, scientists believe further research using stem cells offers great promise that could help improve the lives of those who suffer from many terrible diseases -- from juvenile diabetes to Alzheimer's, from Parkinson's to spinal cord injuries. And while scientists admit they are not yet certain, they believe stem cells derived from embryos have unique potential.

You should also know that stem cells can be derived from sources other than embryos -- from adult cells, from umbilical cords that

are discarded after babies are born, from human placenta. And many scientists feel research on these types of stem cells is also promising. Many patients suffering from a range of diseases are already being helped with treatments developed from adult stem cells.

However, most scientists, at least today, believe that research on embryonic stem cells offer the most promise because these cells have the potential to develop in all of the tissues in the body.

Scientists further believe that rapid progress in this research will come only with federal funds. Federal dollars help attract the best and brightest scientists. They ensure new discoveries are widely shared at the largest number of research facilities and that the research is directed toward the greatest public good.

The United States has a long and proud record of leading the world toward advances in science and medicine that improve human life. And the United States has a long and proud record of upholding the highest standards of ethics as we expand the limits of science and knowledge.

Research on embryonic stem cells raises profound ethical questions, because extracting the stem cell destroys the embryo, and thus destroys its potential for life.

Like a snowflake, each of these embryos is unique, with the unique genetic potential of an individual human being.

As I thought through this issue, I kept returning to two fundamental questions: First, are these 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?

I've asked those questions and others of scientists, scholars, bioethicists, religious leaders, doctors, researchers, members of Congress, my Cabinet, and my friends. I have read heartfelt letters from many Americans. I have given this issue a great deal of thought, prayer and considerable reflection. And I have found widespread disagreement.

On the first issue, are these embryos human life -- well, one researcher told me he believes this five-day-old cluster of cells is not an embryo, not yet an individual, but a pre-embryo. He argued that it has the potential for life, but it is not a life because it cannot develop on its own.

An ethicist dismissed that as a callous attempt at rationalization. "Make no mistake", he told me, "that cluster of cells is the same way you and I, and all the rest of us, started our lives. One goes with a heavy heart if we use these", he said, "because we are dealing with the seeds of the next generation."

And to the other crucial question, if these are going to be destroyed anyway, why not use them for good purpose -- I also found different answers.

Many argue these embryos are by-products of a process that helps create life, and we should allow couples to donate them to science so they can be used for good purpose instead of wasting their potential.

Others will argue there's no such thing as excess life, and the fact that a living being is going to die does not justify experimenting on it or exploiting it as a natural resource.

At its core, this issue forces us to confront fundamental questions about the beginnings of life and the ends of science. It lies 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.

As the discoveries of modern science create tremendous hope, they also lay vast ethical mine fields.

As the genius of science extends the horizons of what we can do, we increasingly confront complex questions about what we should do. We have arrived at that brave new world that seemed so distant in 1932, when Aldous Huxley wrote about human beings created in test tubes in what he called a "hatchery."

In recent weeks, we learned that scientists have created human embryos in test tubes solely to experiment on them. This is deeply troubling, and a warning sign that should prompt all of us to think through these issues very carefully.

Embryonic stem cell research is at the leading edge of a series of moral hazards. The initial stem cell researcher was at first reluctant to begin his research, fearing it might be used for human cloning. Scientists have already cloned a sheep. Researchers are telling us the next step could be to clone human beings to create individual designer stem cells, essentially to grow another you, to be available in case you need another heart or lung or liver.

I strongly oppose human cloning, as do most Americans. We recoil at the idea of growing human beings for spare body parts, or creating life for our convenience.

And 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.

My position on these issues is shaped by deeply held beliefs. I'm a strong supporter of science and technology, and believe they have the potential for incredible good -- to improve lives, to save life, to conquer disease. Research offers hope that millions of our loved ones may be cured of a disease and rid of their suffering. I have friends whose children suffer from juvenile diabetes. Nancy Reagan has written me about President Reagan's struggle with Alzheimer's. My own family has confronted the tragedy of childhood leukemia. And, like all Americans, I have great hope for cures.

I also believe human life is a sacred gift from our Creator. I worry about a culture that devalues life, and believe as your President I have an important obligation to foster and encourage respect for life in America and throughout the world.

And while we're all hopeful about the potential of this research, no one can be certain that the science will live up to the hope it has generated.

Eight years ago, scientists believed fetal tissue research offered great hope for cures and treatments -- yet, the progress to date has not lived up to its initial expectations. Embryonic stem cell

research offers both great promise and great peril. So I have decided we must proceed with great care.

As a result of private research, more than 60 genetically diverse stem cell lines already exist. They were created from embryos that have already been destroyed, and they have the ability to regenerate themselves indefinitely, creating ongoing opportunities for research.

I have concluded that we should allow federal funds to be used for research on these existing stem cell lines, where the life and death decision has already been made.

Leading scientists tell me research on these 60 lines has great promise that could lead to breakthrough therapies and cures. This allows us to explore the promise and potential of stem cell research without crossing a fundamental moral line, by providing taxpayer funding that would sanction or encourage further destruction of human embryos that have at least the potential for life.

I also believe that great scientific progress can be made through aggressive federal funding of research on umbilical cord placenta, adult and animal stem cells which do not involve the same moral dilemma. This year, your government will spend \$250 million on this important research.

I will also name a President's council to monitor stem cell research, to recommend appropriate guidelines and regulations, and to consider all of the medical and ethical ramifications of biomedical innovation.

This council will consist of leading scientists, doctors, ethicists, lawyers, theologians and others, and will be chaired by Dr. Leon Kass, a leading biomedical ethicist from the University of Chicago.

This council will keep us apprised of new developments and give our nation a forum to continue to discuss and evaluate these important issues.

As we go forward, I hope we will always be guided by both intellect and heart, by both our capabilities and our conscience.

I have made this decision with great care, and I pray it is the right one.

Thank you for listening. Good night, and God bless America.

President Bush had changed his position on federal funding of stem cell research. However, the major restriction was that researchers could only use cells from existing embryonic stem cell lines, **for which the life and death decision had already been made**, so that no more embryos would be killed.

Allowing any funding would upset some; restricting research to existing lines would upset others; and not allowing unrestricted research would upset still others. Politically speaking, Bush may have done the very best he could do, as Congress would have almost certainly overridden any decision to prohibit the governmental sponsored stem cell research altogether. From this vantage point, Bush may deserve to be commended, however, the question remains as to whether his decision is morally praiseworthy.

The Center for Bioethics and Human Dignity felt that the moral line that Bush had set may be extremely difficult to hold. Acknowledging that human life is a “sacred gift from our Creator” which should not be devalued, Bush arrived at a policy which would fund research on stem cells obtained from embryos for whom the life and death decision had already been made. **The implication is that by supporting the research only on embryos who have already been destroyed, the government can simultaneously distance itself from any endorsement of embryo destruction.**

The Center suggests that there are two sets of questions to be addressed. First, one needs to determine whether they are, at the most basic level, opposed to the killing of embryos. If they are, but an embryo has already been destroyed despite their opposition, may they support the research on the resulting stem cells and still be regarded as morally upright? Or, are those in favour of the experimentation necessarily also aligned with the tragic loss of embryonic life? Should they condemn such experimentation because of their basic objection to the sacrifice of human embryos for use in medical research since that is what is occurring regardless of who was directly responsible for carrying out the sacrifice.

They suggest that however one resolves these challenging questions, we should agree to never cross what Bush has called the “fundamental moral line of providing taxpayer funding that would sanction or encourage further destruction of human embryos.” Whether that line is crossed will depend on the political climate and on how the science of stem cell research advances over the next several years.

Some characterized President Bush’s decision to limit embryonic stem cell studies to existing sets of stem cell lines as being a cruel

compromise. Researchers said that only by studying stem cells from many different embryos, can science be sure that treatments developed would be universally available. By limiting the number, they said there was a risk of creating two biological classes - those who can be treated by stem cell therapy and those who cannot.

There was also the question of whether there were actually 60 or more usable stem cell lines. Some scientists have estimated that there were only 12 stem cell lines including some that would not meet strict research guidelines. At the time of Bush's speech, the only publicly known stem cell lines were 5 at the Rambam Medical Research Centre in Israel, 4 at the University of Wisconsin and 4 derived by BresaGen Inc. in Australia.

On August 28, 2001, the National Institutes of Health announced and identified 10 labs that had developed 64 embryonic stem cell lines and that these were approved for use in government funded research. The eligible cell lines were developed at four U.S. labs, at two labs each in India and Sweden and at one lab each in Australia and Israel. Goteborg University in Sweden had the most stem cell lines with a total of 19.

CyThera Inc. of San Diego has 9 cell colonies and company officials said their first cell line would be ready for use by other researchers in 2002. The University of California has 2 cell lines which are expected to be available to researchers within months. The Monash Institute of Reproduction and Development in Australia has 6 cell lines and 50 research applications had already been filed with it to conduct research. BresaGen Inc. in Australia has 4 cell lines but company officials said the guidelines have not been drawn up to give access to outside researchers. The Wisconsin Alumni Research Foundation, which holds the patent for 5 cell lines, along with a patent on a method for extracting and

culturing stem cells, said it already had provided colonies of cells to about 30 researchers. **The Foundation charges \$5,000 for two vials each containing about 1 million stem cells. The price is considered to be a modest break-even.**

Although this silenced some of the scepticism, many experts still contended that 64 lines may not be adequate. They believe there is a question about the quality of the cell lines and if they are of sufficient genetic diversity for scientists to do the work that needs to be done.

The White House reacted by noting that all the stem cell research currently being done on mice is being done on only 5 stem cell lines and that with 60 stem cell lines available, there would be enough work to keep the scientific community very busy and hopefully producing cures.

Notwithstanding, the researchers insisted that even 60 cell lines is not enough and that it would take hundreds of embryonic cell lines to harvest the full benefit of stem cell therapy. The principal reason for this view is that since the embryonic stem cell lines come from different embryos, they have fundamental genetic differences that may not be compatible with the immune system of the receiving patient. Without this compatibility, the body would reject curative cells.

Dr. Harold Varmus is a Nobel laureate and former head of the National Institutes of Health. He agrees that limiting embryonic cell lines could be a cruel compromise for some people. He noted that there is going to be a need to have a sufficiently large repertoire of cell lines to treat patients who have very different types of immune sensitivities.

He also suggested that cell lines would be a poor investment if science ended up the stem cells that would not be compatible with the patients. He estimated that it could take research with hundreds of cell lines to assure that developed treatments could be used by nearly everyone.

In responding to the moral arguments, Health and Human Services Secretary, Tommy Thompson, said that Bush's decision was moral because it will allow federally financed research only on embryos that have been destroyed by the time of the announcement. "Are we just going to throw them in the garbage can and say there's nothing that can be done on them? You can't put them back together." He also noted that the federal government already funds research on umbilical cord, placenta, adult and animal stem cells.

Other reactions to President Bush's decision were as follows:

- Since we know that different embryonic stem cell lines have different properties, why do we think that the very first lines to be derived have the best properties?
- Researchers do not know the minimum number of cell lines needed to get the maximum benefit. We really won't know until we start working with cell lines.
- Limiting the number of cell lines discourages creation of new cell lines.
- The number of cell lines is so small that if an accident occurred it could knock out a major part of the cell lines which would be a disaster for public policy.
- The U.S. bishops were quick to condemn the very idea of accommodating the intentional destruction of human embryos

for research calling it “morally unacceptable”. Bishop Joseph Fiorenza, President of the National Conference of Catholic Bishops characterize the existing stem cell lines as “ill-gotten goods” and stated that: “For the government to allow funding for this experiment makes the government complicit in what we consider to be wrong doing. The federal government, for the first time in history, will support research that relies on the destruction of some defenceless human beings for the possible benefit to others. It allows our nation’s research enterprise to cultivate a disrespect for human life.”

- Pope John Paul II had exhorted the president to reject embryonic stem cell research stating that: “A free and virtuous society, which America aspires to be, must reject practices that devalue and violate human life at any stage from conception until natural death.”
- The fact that he is not putting federal funds in support of killing additional human beings is a very critical line not crossed.
- The federal government, for the first time in history, will support research that relies on the destruction of some defenceless human beings for the possible benefit of others. It allows our nation’s research enterprise to cultivate a disrespect for human life.
- It was naive to think that Bush’s spiritual concerns would completely outweigh his political ones.
- There is nothing wrong with going slow. Bush basically said he wants this research to proceed slowly but carefully.
- Scientists pressed for more latitude to avoid possible treatment delays. They said that this was the first time they learned that

there were about 60 lines available. They expressed concern that the number was much smaller and wanted to know how these lines materialize, who has some, where the scientific reports on them are and how good are they.

- Political conservatives urged restraint despite declarations by some that the restriction would slow and perhaps even cripple promising medical research.
- Dr. John Gearhart, a researcher at Johns Hopkins University in Baltimore said he was disappointed in the limited funding to only 60 lines of existing stem cells suggesting that it put a substantial delay on the progress needed to bring these types of therapies to the bedside. He also noted that there is a shelf life to these cell lines which means that more lines will be needed in the future.
- Carl Feldbaum, President of the Biotechnology Industry Organization, said the limitation on stem cell lines may place roadblocks to medical progress and may cost years, even lives by delaying potential treatment for many diseases.
- James Thomson, the University of Wisconsin researcher who became in 1998 the first to isolate human embryonic stem cells, said that the proposed compromise will slow the research, but the compromise is better than halting the research entirely.
- Some religious leaders hailed the Solomon-like decision as an ideal solution for a national moral dilemma.
- **Dr. Leon Kass from the University of Chicago and Chair of the President's Council on Bioethics estimated that the 60 existing stem cell lines should last at least a decade.**

The controversy continues on a number of fronts. Congress is looking into the issue of the 64 stem cell lines and the Senate is debating a change to stem cell policy. Essentially, the amendment would allow couples to donate unused embryos from fertility clinics for research purposes. In reply, President Bush reaffirmed that he laid out what he thought was right for America and announced that any piece of legislation that undermines what he thinks is right will be vetoed.

After you have heard from the advocates and all sides of the issue, it is often worthwhile to check out the political commentary in the media.

On August 10, 2001, columnist Scott Rosenberg wrote what I suspect most objective analysts were thinking. He started off by saying that President Bush's non-decision on funding for stem cell research isn't simply the political compromise it is being taken for: **It's a moral fumble that hides the essential cowardice behind sanctimonious rhetoric about "vast ethical minefields" and "profound ethical questions."**

He goes on to characterize the Bush announcement as a split-the-difference decision that seems to offer something to both sides. Supporters of research will at least get some funding and opponents should be placated that no further embryos will be destroyed in the cause of medical research.

But that's where the logic of Bush's decision falls apart according to a commentary. The fact is that thousands of embryos were destroyed each year before stem cell research was an option, and thousands will continue to be destroyed each year no matter what Bush decided.

These embryos are a by-product of in vitro fertilization techniques that are in widespread use today. The important question is why are

human embryos are by-products of any process? If it is unethical to destroy embryos by harvesting stem cells, is it not also unethical to produce surplus embryos.

The House of Commons Standing Committee on Health raised this very issue in their report to the Minister of Health in which they recommended research be conducted on how to safely freeze female eggs. Presumably, this would limit the number of fertilized embryos produced to those that were necessary for the in vitro fertilization procedure and therefore eliminate the creation of surplus embryos. This will undoubtedly continue to be a major point for discussion among legislators and the general public.

QUOTABLE QUOTES

While it is unethical to end life in medical research, it is ethical to benefit from research where life and death decisions have already been made.

President George Bush, August 12, 2001 (Commenting on his decision to restrict stem cell research funding existing cell lines where the embryo was no longer viable)

History has shown that it is always the dispossessed, those whose lives are easily overlooked, who are subjected to the worst abuses of scientific research. So-called “spare” human embryos are particularly vulnerable to this kind of moral blindness because so many people seem to have difficulty identifying with their humanity.

Chicago Archbishop Francis E. George, August 10, 2001

Science confirms that adult stem cells are in fact more chameleon-like than previously suspected, taking cues from their cellular environment to produce offspring of the same type as the cells that surround them. Even lone neural adult stem cells displayed the ability to differentiate themselves into various cell types.

American Association for the Advancement of Science, June 2, 2000

A free and virtuous society, which America aspires to be, must reject practices that devalue and violate human life at any stage from conception until natural death. In defending the right to life, in law and through a vibrant culture of life, America can show the world the path to a truly humane future in which man remains the master, not the product, of this technology.

Pope John Paul II, July 23, 2001

Chapter 6

INTERNATIONAL STATUS

Stem cell research has been a controversial subject for many years around world. The scientific advances have been enormous over a short period of time and the hype surrounding the potential for wide ranging cures and treatments is literally at a fever pitch.

If this new technology meets even its lowest expectations, it will revolutionize health science more than any other development in our history. **This is big business and the research community knows it.** For that reason, research on stem cells has often been characterized as the scientific race of the century.

Needless to say, scientists and pharmaceutical companies everywhere are scrambling to get their stem cell efforts together. Notwithstanding the promising technology, there continues to be a diversity of policies and regulations throughout the international community.

In the United States, stem cell research is not only permitted but a vibrant industry. In August 2001, President George Bush reversed the Clinton administration's position on unrestricted funding of stem cell research. As a compromise, President Bush decided to permit federal funding only for existing stem cell lines for which the life and death decision had already been made.

When stem cells are harvested from embryos, the embryo ceases to be a viable human being and is discarded. The stem cells are then

induced to become a variety of specialized lines of stem cells which would have the ability to become a variety of tissues.

According to the U.S. National Institutes of Health, there are 64 stem cell lines which currently exist around the world and it is estimated that the stem cell lines are sufficient to keep the research community busy for at least a decade. For that reason, Bush restricted federally funded stem cell research to these 64 lines. That means that surplus embryos from in vitro fertilization could not be used for research qualifying for federal funding.

This is not a ban, however, since privately funded research can still utilize the surplus embryos. The U.S. position is considered to be a compromise since it permits researchers to receive funding while at the same time lactating those who have moral and ethical concerns by ensuring that no federal funding will support research where more embryos will be destroyed.

The situation in the United Kingdom is somewhat different. Under the 1990 Human Fertilization and Embryology Act, research was permitted on donated embryos only for strictly limited purposes, including studies on infertility and the detection of birth defects.

However, on January 22nd, 2001, Britain passed a law that goes beyond even President Clinton's position. **The House of Lords voted to legalize the creation and destruction of embryos for stem cell research and to allow the creation of embryonic clones for stem cell research.** Their decision makes Britain the first country to effectively legalize the creation of cloned human embryos but the creation of babies by cloning would remain outlawed.

They also required that a commission look at the ethics of all stem cell research on an ongoing basis. In debate, many were concerned

that ethical worries were being sidelined in the race to be at the forefront of medical research. They proposed an amendment that would have withheld approval of the government's proposal until after the ethical, moral and scientific issues surrounding the research had been studied by a specially created Committee. The amendment was defeated by 212 votes to 92, with the Lords saying the ethical issues should be debated by a special committee at a later date.

The House of Lords heard during the debate that it could take up to a year before the first research permits were granted and that a breakthrough in the field could take a further 10 years. However, U.K. scientists estimated that would be quite likely that the first human trials, probably for a brain disease like Parkinson's, could take place in the next three years. If successful, they see clinical application in five to seven years.

The U.K.'s legislation did however hit a bump in the road on November 15, 2001 when a judge ruled that the government was wrong in thinking that existing laws prevented scientists using the technique that produced Dolly the sheep in attempts to clone people.

Before the High Court, it had been argued that human embryos created by the "Dolly" technique, known as cell nuclear replacement, were not covered by the Human Fertility and Embryology Act of 1990 which regulates the use of embryos created during fertility treatments. Mr. Justice Crane agreed, ruling that an organism created by cell nuclear replacement was not defined as an embryo under the act and that the technique could not therefore be outlawed.

Fearful that unethical doctors could exploit the situation to carry out human cloning research in Britain, the government launched an appeal against the ruling. New laws to ban human cloning would be rushed through Parliament to plug the loophole exposed by the High Court if the government appeal was not successful.

On November 26, 2001, emergency legislation to ban the creation of cloned human offspring, which was characterized as “unsafe and unethical”, cleared the House of Lords and was sent to the House of Commons. The Bill passed on November 30, 2001.

The Human Reproductive Cloning Bill prohibits implanting cloned embryos in a womb. It should be noted that the bill does not prohibit human cloning, only the implantation of cloned embryos. The wording means scientists would still be allowed to use cloning to create embryos for stem cell research. This is the process that was used by Advanced Cell Technologies Inc. in the United States.

The confusion over the law has created a dilemma for the scientific community. How could they continue research on cloned embryonic stem cells while banning cloning for reproductive purposes? The first one is vital to find cures for degenerative diseases while the latter is ethically objectionable.

This is the first serious attempt to clarify the separation between the two different types of research. It should be noted that in America, there is no federal law banning human cloning. It is also estimated that **over 170 nations of the world have no legislation whatsoever preventing the birth of human clones.**

In Europe, there is a mixed picture. In Germany, all forms of embryonic research are prohibited. In France, embryonic research is theoretically permitted if it benefits the embryo. In effect that is a

ban. Generally in Europe, you cannot do therapeutic cloning (stem cell research). That is why Britain is so attractive to scientists.

However, on November 29, 2001, the European Parliament rejected a move to ban cloning in the European Union in a 316 to 37 vote. The move could have interfered with the EU's plans to spend 2.15 billion euros (\$1.91 billion US) over the next four years on health-related genetic research. Approximately 300 million euros of this will go to research on aborted embryos and those left over from in vitro fertilization.

It should be noted that the European Commission, the EU's executive, only supports funding stem cell research that does not involve the creation of human embryos for research purposes. The Commission is against human cloning. The EU is planning to set aside a total of 17.5 billion euro (\$15.38 billionUS) for research over the next four years.

The parliamentary issue came up on the same day as Germany's National Ethics Committee decided to recommend allowing the import of human stem cells from abroad under clear supervision. Cloning of human embryos for therapeutic research is illegal in Germany but if the government accepts the committee's recommendation, researchers will be able to import existing cell lines grown from embryos outside the country.

Nine of the 15 EU states have banned human cloning on a national level. Austria, Germany, France and Ireland banned all embryo research and France is considering changing its law to open up the possibility of stem cell research. Spain and Finland allow embryo research under certain conditions and in Denmark, scientists may only conduct infertility research on embryos.

In Sweden, embryo research is allowed and researchers may also create embryos for research if the project is approved by an ethics commission. Any European ban would have been symbolic since it is up to the individual states to decide their policy but the EU decision could have significant influence over future funding debates.

In Australia, their constitution devolves most of the health legislation to its States. Generally in Australia, it is illegal to take cells from human embryos, the source of many stem cells coveted by research, but it is legal for the cells to be obtained from another country and then used in Australia.

An Australian company called BresaGen purchased a supply of cells from WiCell, a non-profit organization set up by an alumni group at the University of Wisconsin. This is the only center that supplies isolated embryonic stem cells, the only kind that can be grown in culture and then proliferate indefinitely.

In Japan, the government passed legislation related to human cloning which took effect in June 2001. The Japanese law prohibits the transfer of embryos created by techniques of human cloning and those created by mixing human and animal cells into the uterus of a woman or an animal. However, it allows application of these techniques and other similar ones for research purposes as long as the embryo created is not allowed to be transplanted into a human or an animal.

In addition on August 1, 2001, a Japanese cabinet panel on science and technology approved guidelines for research using human embryos. While the law bans human cloning, the approved guidelines would allow scientists to use human embryos created by infertility treatments for experimentation.

On July 30th, 2001, the Russian government passed a temporary ban on human cloning to last for five years. Xinhua news service also reported that the chairman of the scientific council of the Russian national program Human Genome told reporters that the Russian government has also forbidden the import and export of cloned human embryos.

In India, researchers plan to capitalize on President Bush's funding restrictions on embryonic stem cells by moving ahead with their own projects. Two Indian research organizations possess colonies of embryonic stem cells, known as cell lines, which can develop into many of the types of tissues to be used for various new medical procedures. India is only beginning to formulate policies covering stem cell research and there are no legal guidelines currently in place.

On September 28, 2001, Switzerland's National Science Foundation altered its stance on research with human embryos to allow the practice. Approval was given to a Geneva research project which aims to import embryonic stem cells from the United States. The foundation restricted the research to projects that were approved by the scientific panel and were not for commercial purposes. As well, the projects must use stem cells obtained legally, and at no charge, from countries where they were developed for in vitro fertilization purposes and permission has been obtained from the donors.

On December 18, 2001, Communist China joined Britain in allowing human cloning. While both countries say they will not allow reproductive cloning, the result of the legislation will destroy human embryos created by cloning. News reports state that in China restrictions such as banning research on embryos and presumably therapeutic cloning are not being contemplated.

Yanguan Wang, an ethicist who is helping to draft new research guidelines for the Ministry of Health, said that the government may choose not to fund certain controversial research but it will not be prohibited.

The International consensus is “no” to reproductive cloning and mixed to embryonic stem cell research. However, the policy positions are fluid and there are still many countries waiting to for more results on adult stem cells.

QUOTABLE QUOTES

There is no doubt that on your vote, my lords, depends whether some people in the near future get the treatment which might save them from disease or, even worse, death.

Lord Winston, Chairman of the House of Lords Science and Technology Committee

(Debating stem cell legislation, January 22, 2001)

I'm just trying to help people who are sick, and really that's our focus. We're talking about human cellular life, not a human life.

Dr. Michael West, President of Advanced Cell Technologies Inc. (Commenting on their being the first researchers to clone a human embryo-November 25, 2001)

Guiding embryonic stem cells to transform themselves requires a complex and carefully timed addition or removal of special proteins. In general, the hard part is keeping these embryonic stem cells from differentiating. Holding them back is difficult. Once they go, they go in many directions.

**Dr. James A. Thompson, researcher,
University of Wisconsin August 10, 2001**

Our data has indicated that cells generated by cloning will be completely rejuvenated, allowing us to envision not only treatment, but prevention of all age-related diseases. A recent study on the impact of this technology on human health estimates that more than 125 million U.S. Americans can benefit from embryonic stem cell related treatments.

(Testimony before the Standing Committee on Health)

Mr. Jose Cibelli, VP Research, Advanced Cell Technologies Inc. (Boston, MA)

Chapter 7

CANADA'S LONG ROAD

It has been over ten years since the 1989 Canadian Royal Commission on New Productive Technologies began its work. It has also been five years since the Government of Canada brought forward its last related legislation, Bill C-47, which died on the Order Paper when Parliament dissolved with the call of the 1997 General Election.

When you consider the frenzy of research activity in the area of reproductive technologies, some of which is highly controversial, it is hard to understand why there has been such a delay in introducing the necessary legislation to provide national guidelines. Legislators have fallen dangerously behind the research community who, in the absence of a regulatory framework, have advanced to a point where it may not be possible to reel them back in.

In April 2001, Health Minister Allan Rock asked the House of Commons Standing Committee on Health to conduct public hearings on draft legislation on reproductive technologies and related research. This legislation is largely based on the work of the Royal Commission and was crafted by the Canadian Institutes for Health Research.

The following is the Preamble from the document "Proposals For Legislation Governing Draft Legislation On Assisted Human Reproduction":

Whereas the Parliament of Canada

acknowledges the benefits to individuals and to society in general of assisted human reproductive technologies;

believes that those benefits can be most effectively secured by taking appropriate measures for the protection and promotion of human health, safety, and rights in the use of such technologies;

appreciates the paramount need for measures to protect and promote the best interests of children affected by the application of those technologies;

recognizes that, while all persons are affected by those technologies, women more than men are directly and significantly affected by their application;

wishes to promote the principle of free and informed consent as a functional condition of the use of human reproductive technologies;

recognizes the health and ethical concerns inherent in the trade in the reproductive capacities of women and men, and in the exploitation of children, women and men for commercial ends;

recognizes the importance of preserving and protecting human individuality and the integrity of the human genome;

NOW, THEREFORE, Her Majesty, by and with the advice and consent of the Senate and House of Commons of Canada, enact the Assisted Human Reproduction Act.

The preamble embodies a powerful set of core values and principles which should guide the development of regulations and the interpretation of the legislation. **It does not, however, declare the principles or values to be used as guides over the most contentious aspect of the Bill, namely, the destruction of human embryos for research and when human life begins.**

The draft legislation presents both prohibited activities and control activities. Prohibited procedures include the following:

No person shall knowingly:

- create or participate in the creation of a human clone or transplant or participate in the transplantation of human clone into a human being;
- alter the genome of a cell of a human being or in vitro embryo such that the alteration is capable of being transmitted to its descendants;
- maintain an embryo outside of the body of a woman after the 14th day of its development following fertilization or creation, excluding any time in which its development has been suspended;
- create an in vitro embryo solely for purposes of research;
- create, or participate in the creation of, an embryo from a cell or part of the cells taken from an embryo or fetus, or transplant or participate in the transplantation of such an embryo into a human being;

- transplant sperm, and ovum, embryo or fetus of an animal into a human being;
- for the purpose of creating a human being, make use of any human reproductive material that is or was transplanted into an animal;
- perform any procedure or provide, prescribe or administer anything for the purpose of assuring or increasing the probability that an embryo will be of a particular sex, except for reasons related to the health of the resulting human being.
- offer to do, or advertise the doing of, anything prohibited by the legislation and
- pay or offer to pay any consideration to any person for doing anything prohibited by the legislation.

The legislation also prohibits payments for surrogacy, the purchase of gametes (sperm and ova), the purchase of other reproductive material, the use of reproductive material without consent, the posthumous use of reproductive material without consent, the use of an embryo without consent, obtaining gametes from a minor and the use of minor's gametes.

The proposed controlled activities include:

- No person shall, except under licence, alter, manipulate or treat any human reproductive material for the purpose of creating an embryo or facilitating human reproduction.

- No person shall, except under licence, make any use of any in vitro embryo, or part of one, for the purpose of research or the prevention, diagnosis or treatment of disease, injury or disability.
- No person shall, except under licence, collect, store, transfer, destroy, import into Canada or export from Canada any sperm, ovum, or in vitro embryo for the purposes referred to above.
- No person shall, except under licence, create a chimera (i.e. combination of animal and human cells or material) for any purpose including research.
- No person shall, except under licence, combine any part or any proportion of the human genome specified in the regulations with any part of the genome of an animal species specified in the regulations.

The balance of the draft legislation addresses Administrative, Privacy and Confidentiality, and Inspection and Enforcement provisions.

On May 3, 2001, Health Minister Allan Rock appeared before the Standing Committee on Health to present the draft legislation. As part of his presentation, the minister stated the following: **“There must be a higher notion than science alone that can guide scientific research and endeavour. Simply because we can do something does not mean that we should do it”**. Needless to say, the minister’s statement squarely hit the target in identifying that there were serious contentious questions to be addressed by the hearings.

Under prohibited procedures, paragraph 3.(1)(c) states that no person shall knowingly maintain an embryo of outside the body of a woman after the 14th day of its development following fertilization or creation, excluding any time in which its development has been suspended (referring to the time during which an embryo is frozen).

This is consistent with the 1993 report of Canada's Royal Commission on New Reproductive Technologies. They recommended that there should be no experimentation on zygotes / embryos after 14 days, the point that marks the development of the primitive streak, which fixes the individual identity of the embryo and forms the basis for its nervous system.

During the hearings before the Health Committee, Health Canada officials also stated that the research on in vitro human embryos would be strictly regulated because of their special status, namely, their **potential to become human beings**. This entire issue is problematic for those who believe that human life starts at conception and that morally it is wrong to kill an embryo.

The following are extracts of the testimony from three witnesses who commented on this matter before the House of Commons Standing Committee on Health on November 1, 2001:

1. The draft legislation puts a 14-day limit on the use of embryos for the purposes of research. This 14-day limit has a long history but it has no clear basis in my view. The reasons given for the 14-day limit are that it's when the primitive streak appears; it's when the primitive

nerve cells start; it's when twinning is no longer possible, so you have a unique individual; and its when implantation is no longer possible. But when you have some many disparate reasons, you have difficulty in justifying that cut-off is indicated. You still might want to use it, but at least recognize that **there is no clear reason for using it.** (Dr. Margaret Somerville, Acting Director, McGill Centre for Medicine, Ethics and Law)

2. Last week, all the ethicists agreed that the human embryo is a human being and we agree the embryo and fetus are not mere human organisms and even the *Tri-Council Policy Statement for Ethical Conduct in Research Involving Humans* attributes a special moral status to the embryo. (Mr. Bruce Clemenger, The Evangelical Fellowship)
3. In our view, a human being exists from conception. That position is shared by medical and other professional opinions. The Law Reform Commission of Canada, for instance, in its working paper "Crimes Against the Fetus", more than 10 years ago affirmed that a human being exists from conception. As they wrote: "True, the present code has a curious provision in Section 206 to the effect that a child doesn't become a human being until it has proceeded completely from its mother's body. This, far from being a proper definition of the term, runs counter to **the general consensus that the product of human conception, in the womb or outside, is a human being.**" The human being is to be respected and treated as a person from the moment of conception. This key principle of Catholic teaching, of respecting and protecting human life from its earliest existence, has obvious ramifications. (Dr. Bridget Campion, St. Augustine's Seminary)

The moral question of when human life begins is the single most controversial issue concerning embryonic stem cell research. When you consider public attitudes towards embryos created by in vitro fertilization to assist infertile couples, it is hard to imagine someone dismissing them as just cells. In vitro fertilization is by far the best testament to the fact that human life begins at conception. There is a maxim in ethics which holds that **where there is a conflict between the ethically unacceptable and the scientifically possible, the ethical view must prevail.**

The Committee heard from a number of very good witnesses on a broad range of subjects. Two other witnesses addressed important considerations which most others seemed ignored. The first was Dr. Ronald Worton of the Ottawa Health Research Institute who made the following statements:

“One argument that’s been made is that since adult stem cells are capable of making these various tissues, why don’t we just use adult stem cells for research and for the eventual treatments? Why do we even need to work with embryonic stem cells at all? The answer is that, in the end, we hope it will be the case that adult stem cells will be the source of all cells we use for therapeutic purposes, and we won’t have to use embryonic stem cells.”

“But right now, we know that embryonic stem cells have a lot more potential. They’re said to be pluripotent—they can make any kind of tissues, and they do it with a high level of efficiency. We know adult stem cells can make certain other tissues, but we don’t know the full spectrum of what they can make. We know they’re not as efficient, and they’re somewhat difficult to grow. So we think there’s an absolute necessity to work with embryonic stem cells and adult stem cells and fully understand the differences between

them if we're ever going to have a hope of utilizing adult stem cells to their full potential."

"There's a group that has formed a network of centres of excellence from across Canada called the Stem Cell Network. We've recently been funded by the federal government for **\$21 million over the next four years**. (Author's note: Mr. Worton has told the media that plans are already under way to build a multi-million dollar stem cell facility in Ottawa next year."

"Research will concentrate mainly on muscular diseases such as muscular dystrophy). One of the main experiments we want to do is to try to understand what the molecular events in a stem cell are. What are the molecular characteristics of an embryonic stem cell, and what are the molecular characteristics of adult stem cell? What are the differences?"

"We think if we understand that, we'll be able to take adult stem cells and manipulate them-add in any molecular factors that are missing, and make them more like an embryonic stem cells. Give it more potential, if you like. But if we don't understand what the factors are in the embryonic stem cells, then we don't have a hope of making adult stem cells behave as though they came from embryos."

Dr. Worton was the only witness who made the point that embryonic stem cell research may help to perfect adult stem cell therapy. He also has disclosed that the federal government has made a significant investment in stem cell research and that a major facility would be built in Ottawa.

This was a big surprise to the Committee members since they had been asked to consult with public presumably with a view to determine whether such matters as embryonic stem cells research

was acceptable. If the Stem Cell Network was already authorized to conduct embryonic stem cell research over the next four years, what would be the point of consulting with the public and other stakeholders?

It should be highlighted that the Committee specifically noted in its report that: **“We are concerned that there is a lack of clarity about what is currently taking place in Canada in relation to research that uses existing embryos or research that creates embryos.”** Legislators and the public should know what is currently going on if they are asked to make informed decisions as to where we can and should go next.

The other testimony of note came from Dr. Michael Rudnicki of the Ottawa Health Research Institute. He was the only witness to address the issue of stem cell supply for proven therapies. Experts have estimated that the 64 stem cell lines already in existence could keep researchers busy for at least a decade. However, the demand for stem cells will be enormous to treat the millions of people who would benefit from proven new therapies. Here is what Dr. Rudnicki had to say:

“I believe there will be an ongoing need for additional cell lines. Embryonic stem cells have a limited life span in culture. They are technically immortal, but what happens is that they accumulate mutations, and there is genetic drift in that population as you passage it and they go off. Fresh embryonic stem cells behave very differently from old stocks, so the naive notion that 60 are sufficient forever is simply untrue. That being said, we will also need a diversity of embryonic stem cells, because with embryonic stem cells, because of those changes that occur, one particular line might be better at making pancreatic beta cells, while another line might be better at making heart tissue. That’s one thing. Also, one

could imagine a need for having a bank of embryonic stem cells that are immunologically matched donors. So there will really be a need for creating these on an ongoing basis. Whether or not the leftover embryos (from IVF) will provide sufficient numbers is debatable.”

The impact on our health system could be enormous and the demand for stem cells could push the system into chaos if we do not establish the necessary control mechanisms. What will it cost? How will it be safeguarded? What accountability will there be? How will we handle informed consent? What about legal liability? How will we ensure that other important research continues? Research to develop new therapies carries with it certain problems but these pale in comparison to the challenges that will emerge once therapies come to market.

The Health Committee completed its hearings in November and on December 12, 2001, they tabled their report entitled ASSISTED HUMAN REPRODUCTION: BUILDING FAMILIES in the House of Commons. The consensus report covers a broad range of issues and raised some serious concerns. Here are a few comments extracted from the report:

- ... The Committee is conscious of the potential for some of the new technologies to contribute to the alleviation of human suffering. It has attempted to establish a framework within which related medical research can pursue this goal, while respecting the deep desire communicated to the Committee by many Canadians that human embryos and other reproductive materials be accorded the respect and dignity which is their due.
- On hearing the multiple ethical, social, legal, scientific, medical, and other perspectives on this complex issue, we

understood the urgent need to establish clear boundaries around efforts to assist human reproduction and to conduct related research. We became more conscious of the tension arising from the potentially conflicting interests between facilitating reproduction and supporting research. Witnesses told us about the many benefits arising from procedures and practices and the potential for more good to come from ongoing research. They also pointed to the possibilities for harm to individuals and society if current directions were left unchecked by legislation and regulation.

- ... We heard that the major goal of the legislation is to protect the vulnerable from adverse health effects and from exploitation connected to assisted human reproduction. In addition, we were told that where there is a conflict between the ethically unacceptable and the scientifically possible, the ethical view must prevail.
- ... Assisted human reproduction is technologically oriented and physically intrusive. With its calculated and deliberate use of human reproductive material and production of human embryos, it impinges on society's sense of uniqueness, worthiness, and wholeness associated with being human.
- ... There must be a measure of respect and protection for the embryo that is based on its potential for personhood.
- ... It is contrary to our thinking to treat human beings or human material as commodities that can be regarded in terms of their economic value rather than their intrinsic worth.

- **...(The legislation should include a guiding principle that) persons with disabilities can lead full and satisfying lives and enrich the lives of those around them.**
- ... The Committee feels strongly that the potential adverse effects, whether physical, psychological or social, for the resulting children are sufficient reason to prohibit reproductive cloning. In addition, “therapeutic cloning” should be banned as it is unsafe as it commodifies, (treats as a commodity), the embryo.
- ... The Committee heard that germ-line genetic alteration is both unsafe and impractical at this time as well as having unknown consequences for subsequent generations. The Committee acknowledges that the intention of germ-line genetic alteration is to affect patterns of genetically based diseases. However, it agrees with the draft legislation that this should also be banned by statute.
- ... The Committee agrees that embryo creation should be prohibited when the sole purpose of creating the embryo is to provide material for research.
- ... The Committee feels strongly that the commodification and commercialization of human gametes and human embryos can have far-reaching social and emotional effects for any resulting families. But, in addition, such activities are contrary to Canadian practice whereby human organs and tissues are not sold or purchased. The purchase, barter or exchange of human gametes and embryos is contrary to human dignity.
- ... The Committee wants to emphasize that the gains to be made in new scientific knowledge and medical applications

should proceed only if any benefit for society does no harm to the resulting children and participating adults. We particularly want to stress that, while science has tremendous potential for good, its applications can have the capability for negative effects on the diversity of the human population. We do not want to support any public policy, scientific research or medical practices that seek to use knowledge of heredity or genetic characteristics to change the intrinsic characteristics of the human population. As stated earlier, the activities permitted by this legislation must recognize the importance of preserving and protecting human individuality and the integrity of the human genome.

- ... We are concerned that there is a lack of clarity about what is currently taking place in Canada in relation to research that uses existing embryos or research that creates embryos.
- ... We heard that while embryonic stem cell research presents some possibilities, other sources such as umbilical cord blood and adult source stem cells are more available, more easily obtainable, and less ethically contentious.
- ... The Committee was struck by testimony that, in the past year, there have been tremendous gains in adult stem cell research in humans. We also heard that, after many years of embryo stem cell research with animal models, the results have not provided the expected advances. Therefore, we want to encourage research funding in the area of adult stem cells.
- ... We are concerned that embryonic stem cells research commodifies the embryo. It involves research that uses

embryos to obtain further research material. We believe that licences for the conduct of all research on embryos should be issued only after clear demonstration that non-embryonic sources would not achieve the sought after research outcomes.

- ... The Committee is particularly concerned about the excess number of embryos that may be produced and stored, allegedly for reproductive purposes. We appreciate that, until egg-storage techniques are perfected, an excess number of embryos may have to be produced. However, we expect this practice to cease once the storage technology has been validated. At that time, it will be possible to limit the number of embryos produced to those actually used for implantation.
- ... Clause 40(1)(M) allows regulations to be made that would essentially exempt a class or classes of control activities from the application of the legislation or regulations. The Committee joins the witnesses in believing that subordinate legislation, namely regulations, should not be able to override the provisions of the statute. If there is a need to create exemptions, these should be enacted through legislative amendments subject to full parliamentary scrutiny.
- ... The Committee recommends that ... all proposed regulations be laid before the House of Commons for approval or modification within 30 sitting days. ... Given that assisted human reproduction and related research is such a highly sensitive and controversial area, we strongly feel that a parliamentary safeguard of this nature is necessary. Elected representatives should have the

opportunity to shape essential regulations to ensure that they reflect the best interests of Canadians.

- ... Because of the rapidly changing scientific and technological environment, we feel that a parliamentary review within three years (rather than 5 years) would be more appropriate. The subject matter of this legislation is highly sensitive and controversial. Parliament must carry out an earlier, more timely review to insure that the legislation is still in tune with the changing times and technologies.
- ... The Committee heard that precautionary measures must be taken to reduce infertility. In our view, preventing some of the risk factors contributing to infertility would be more appropriate than developing new medical interventions to bypass the infertility that may result from exposure to sexually transmitted diseases, occupational and environmental exposures or even postponement of pregnancy.
- ... For consistency and clarity, we believe that all definitions should be together at the beginning of the legislation. In addition, we find the term “human reproductive material” offensive in its inclusion of “embryo”.
- ... The Committee is seriously concerned about the patentability of human material. We are deeply disturbed that the Patent Act does not specifically disallow patenting with respect to human genes, DNA sequences and cell lines.

The Health Committee made 36 recommendations and requested a response from the Minister within 150 days. It should be noted that on January 15, 2002, The Honourable Anne McLellan became the new Health Minister. There is no reason to believe that the Minister will not be able to respond on time but for a variety of reasons, the response may be very problematic considering the demands of the Committee.

Many Committee members were torn between the ethical concerns of embryonic stem cell research and the potential to advance medicine. They seemed to be leaning towards recommending a moratorium on embryonic stem cell research because the witnesses were very convincing that adult stem cells could be just as effective without the ethical and moral controversy. Instead, in an effort to keep all parties on side, they settled on a compromise to accept embryonic stem cell research but with some onerous recommendations that would seriously restrict the potential use of human embryos.

The Committee recommended that new legislation **incorporating their recommendations** become a priority. However, a number of their recommendations would necessitate major surgery to the draft legislation. Consider the following:

- The Committee opposes the commercialization and commodification of gametes and embryos. This is problematic for the CIHR who boasts that they want to become the supplier to the world.
- They also recommend that licences for the conduct of all research on embryos be issued only after demonstrating that non-embryonic sources would not achieve the sought after research outcomes. This will virtually shut down embryonic research since adult stem cell therapies are advanced for

many practical applications of stem cell therapy without the risk and controversy.

- Also, there are a number of recommendations which would virtually shut down the supply of surplus embryos from in vitro fertilization procedures. This would become a major impediment to sustaining any meaningful research activity.
- They also want all regulations to be subject to review, and approval or modification by parliament which would be generally unacceptable to the government because of the loss of expediency afforded by Governor in Council (i.e. Cabinet) approvals.
- Finally, they want an independent regulatory body, outside the Department of Health to oversee the operation of the Act.

These positions alone will require the government to do some careful thinking as to how they can appease the Committee to ensure that future legislation will pass in the House. This will take some time and may mean that comprehensive legislation may not come forward very soon. According to the Canadian Institutes of Health Research (CIHR), who are responsible for the selection and funding of research, there are no prohibitions on embryonic stem cell research in Canada today. As such they can continue to fund the controversial research even if legislation is not in place.

There is another big hurdle for any federal legislation. Co-operation among federal, provincial and territorial governments is necessary because all levels of government have health responsibilities. For example standards of clinical practice and operation are in provincial jurisdiction.

Co-operation between levels of government has often been a major challenge and the first blow on this issue came on January 11, 2002. **The Province of Quebec announced a ban on all research involving human embryos.** David Cliché, Quebec's Minister of State for Science and Technology unveiled new guidelines on ethical research in which the creation and use of stem cells extracted from human embryos is **forbidden**. They also banned cloning for reproductive and research purposes and other provisions, many of which are in the draft federal legislation.

The most controversial issue remains the ethics and morality of embryonic stem cell research. It appears that there is sufficient consensus for the other main elements of the draft legislation, which are unrelated to research, to proceed and most stakeholders agree that it is urgent that this happen as soon as possible. Now the government must decide on the next step.

If the government is not able come up with timely resolutions and / or compromises to address the Committee's broad concerns and restrictive recommendations, they may choose to proceed with legislation, substantially as is, since most of the legislation is not controversial and is necessary.

Alternatively, they could bring in legislation on the non-offending proposals on reproductive technologies issues such as cloning, surrogacy, genetic alteration etc. To further delay addressing these critical reproductive technology issues is not the preferred option. At the same time, they would have to develop a strategy to defuse the controversies surrounding the destruction of human embryos by informing Canadians of the substantive facts and then seeking a national consensus on how to proceed.

U.S. President George Bush was totally opposed to embryonic research despite the considerable support from those who saw it as

the potential key to curing major illnesses and disease. In the end, the classic political compromise emerged in an effort to create a “win – win” situation. Despite some broad criticism for the decision, the consensus was that Bush did the best he could under the circumstances. In the absence of a Canadian consensus, seeking the “win – win” compromise may prove to be the best option available.

QUOTABLE QUOTES

Medical revolution carries with it moral, ethical and philosophical consequences and our ability to deal with these matters sometimes lags behind our technical knowledge.

**Dr. W. Fox, M.P., British House of Commons,
January 22, 2001**

Our interpretation in the Canadian Institutes of Health Research (CIHR) is that there is nothing to prohibit human embryo research in Canada. Canadians have a strong tradition in animal and adult stem cell research and creating Canadian embryonic human cell lines is an important priority. I think it's likely that we'll be able to generate some of the better cell lines that could be available and useful for people worldwide.

**Dr. Janet Rossant, Chairwoman, Ad Hoc Working Group on
Stem Cell Research, Canadian Institutes of Health Research**

A few people are importing cell lines from Wisconsin and there might be labs starting with fresh embryos and starting to drive around stem cell lines. I don't know of anybody who is driving new lines at the moment but that's only because I haven't made a conscious effort to inquire.

**Dr. Ron Worton, Scientific Director,
Ottawa Health Research Institute**

It was tragic, catastrophic, a real nightmare and we can't turn it off!
(Comment on a disastrous attempt to treat Parkinson's disease with stem cells from a fetus which resulted in uncontrollable shaking)

**Dr. Paul Greene, a neurologist at Columbia University's
College of Physicians and Surgeons**

Chapter 8

THE FINAL WORD

It has been over eight years since the Royal Commission on Reproductive Technologies issued its report. During that time, medical science, in the absence of a legislated regulatory framework, has rapidly developed the ability to create, manipulate and alter human life in ways which can literally redefine what it means to be a human being.

Information from the Human Genome Project and other new research methodologies, will continue to dramatically improve our research and healthcare capabilities over the next decade. As such, the important question is whether we will have the ability to control this research and to ensure that it is safe and not exploited in unintended ways.

Embryonic stem cell research is still in its infancy, and few individuals, either legislators or the general public, have given serious thought to its research, medical, societal, ethical, moral, or religious implications. Some researchers also seem to be exhibiting signs of tunnel vision, seeing only cells but not life, while they advance their work well beyond anything contemplated by public policy makers.

Although embryonic stem cell research has been touted as having great potential for health therapies, it is ethically controversial, not proven in human clinical trials and it has problems with rejection by the immune system.

On the other hand, adult stem cell therapies have already been developed for some practical applications; they are not subject to immune rejection; they are less risky; there are no ethical problems; and they have been safely used in some treatments, such as bone marrow transplants, for many years.

Progress on adult stem cells has great momentum and should receive a high priority in our research efforts. Many believe that it is only a matter of time before these therapies are developed for every practical application. Once that transpires, there will be no need for embryonic stem cell research.

We all want to alleviate suffering and to find cures for illness and disease. However, we do have a responsibility to establish ethical limits to research. The most controversial question is a matter of when life begins and whether it is acceptable to destroy one life for the benefit of others. International consensus recognizes that the human embryo is a human being and that when the ethically unacceptable and the scientifically possible are in conflict, ethics must prevail.

Given the risks and uncertainties associated with new reproductive technologies, governments should not delay in bringing down legislation to establish the regulatory guidelines on matters for which there is a broad consensus among all stakeholders. That consensus presently does not exist for embryonic stem cell research.

Finally, maintaining the public confidence would be substantially enhanced if this highly sensitive legislation was overseen by a regulatory body which is independent of both the biomedical research community and the government.

GLOSSARY OF TERMS

ADULT STEM CELL: any cell taken from mature tissue, regardless of the donor. In general, a cell with the capacity to reproduce itself, and to produce a distinct and differentiated tissue.

ARTIFICIAL INSEMINATION (AI): the injection of collected sperm from a partner or donor into a woman's uterus to fertilize an ovum (egg).

ASSISTED HUMAN REPRODUCTION (AHR): any activity undertaken for the purpose of facilitating human reproduction. Examples of AHR include In Vitro Fertilization, donor insemination and sperm injection.

BLASTOCYST: A pre-implantation embryo of 30 to 150 cells. It consists of an inner cell mass (which develops into the embryo and from which embryonic stem cells may be derived), covered by a thin layer of cells known as a trophoblast.

BLASTOMERE: totipotent stem cells in the human embryo which last no longer than the 19th day following conception.

CELL LINES: cultures of disaggregated tissue that can be maintained and propagated for use in research. The length of time cells will survive in culture (artificial laboratory medium) varies. Some cell lines are immortalized; that is they can be maintained essentially indefinitely for one of a variety of reasons. Embryonic stem cells and embryonic germ cells are immortal because they

express telomerase, one of the factors necessary for cells to propagate normally.

CHIMERA: any organism derived from the mixture of two distinct genetic backgrounds. Although this is possible if two independently fertilized embryos fuse together to form one embryo, the term is most commonly used to refer to the combining of human and animal cells.

CLONING: the intentional creation of one or more genetically identical individuals. The process usually refers to a form of asexual reproduction in which the genome from a cell of an individual is used to generate one or more genetically identical individuals. Two possible methods of cloning are Somatic Cell Nuclear Transfer and Embryo Splitting. In gene technology, cloning refers to the process of producing multiple copies of a single gene or segment of DNA, as in skin or cartilage cloning.

CHROMOSOMES: are very long strands of DNA in our cells which contain over 30,000 genes of our genetic makeup.

COMMODIFICATION: is the treatment of human beings or body tissues and substances as commodities – as a means to an end, not as ends in themselves. Thus commercialization includes commodification, but commodification need not entail a profit motive.

DEOXRIBONUCLEIC ACID (DNA): the genetic material, in the form of a double helix or spiral contained in the chromosomes, with codes for hereditary characteristics.

DIFFERENTIATION: the process by which early unspecified cells acquire the features of specific cells such as heart tissue, liver or muscle.

EMBRYO: The stage of two to eight weeks in human development following the zygote stage and before the fetal stage. (Note that the Canadian draft legislation refers to an embryo as a human organism during the first 56 days of its development following fertilization or creation, excluding any time in which its development has been suspended (e.g.. frozen)).

EMBRYONIC STEM CELLS (ES): stem cells extracted from a human embryo that can develop into any of the body's 210 types of cells.

FERTILIZATION: the union of the sperm and ovum.

FETUS: the stage of human development between eight weeks and birth.

GAMETE: the mature male and female reproductive cell which contains one set of 23 chromosomes (e.g. the male sperm and the female egg).

GASTRULATION: the process in which the cells of a blastocyst organize themselves into an embryo about two weeks after conception.

GENE: the physical and functional unit of heredity which is a segment of DNA located in a specific site on a chromosome. A gene directs the formation of an enzyme or other protein.

GENE THERAPIES: the process of inserting new genetic material into one organism for the purpose of treating or controlling a genetic disease. The therapy only affects the person being treated and not the germ-line cells so that no alterations can be passed on

to future children. Gene therapy is also sometimes referred to as somatic cell therapy.

GENETICS: the study of heredity and the variation of inherited characteristics.

GENOME: all the genetic material contained in the chromosomes of a person's cells containing as many as 100,000 genes. The complete DNA sequence in a full set of chromosomes for a given organism.

GERM CELL: the cell or cell line that produces sperm or ova for reproduction and through which genetic traits or changes can be passed from one generation to the next.

GERM-LINE ALTERATION: the modification of the human genome such that the modification is passed on to descendants.

IN VITRO: in glass; done outside the body.

IN VITRO FERTILIZATION (IVF): mature eggs are removed from a woman's ovaries and placed with sperm in a laboratory dish in order to achieve fertilization. Often the resulting embryo(s) is then transplanted into the woman's uterus.

IN VIVO: done within the living body.

INTRA-CYTOPLASMIC SPERM INJECTION: a variation of IVF treatment where a single sperm is injected into an egg using a microscopic needle. This treatment is used if the male partner has severely impaired or few sperm.

MEIOSIS: the process through which sperm and eggs divide in two to produce a sperm or egg with only 23 chromosomes rather than 46 chromosomes which are present in all our bodily cells.

MULTIPOTENT: refers to stem cells which have differentiated to become more specialized cells with a particular function such as red blood cells or skin cells.

NUCLEUS: the core of a cell that contains the chromosomes.

OVARIES: pair of female sex glands in which egg cells are developed and stored and the hormones estrogen and progesterone are produced.

OVUM (OVA plural): the female sex cell formed in the ovary. The ovum is also referred to as the female egg or oocyte.

PLURIPOTENT: refers to the cell's ability to give rise to virtually any tissue type, but not to a functioning organism.

SEX CHROMOSOME: the X and Y chromosomes that determine sex; XY is male and XX is female.

SOMATIC CELL: any cell in the body that does not become a germ cell (i.e. an ovum or sperm).

SOMATIC CELL NUCLEAR TRANSFER (SCNT): This refers to the technique of inserting the nucleus of a cell from one of the body's tissues into an egg which has had its nucleus removed.

SPERM: the male sex or germ cell.

STEM CELLS: primordial, all-purpose, and undifferentiated cells from which all the body's tissues develop. In general, a cell with the capacity to reproduce itself, and to produce a distinct and differentiated tissue. Human embryonic stem cells (harvested from a viable human embryo) can develop into any of the body's 210 types of cells.

SURROGATE: a woman who carries a pregnancy to term for another. The ova used to create the embryo may be hers, or that of the contracting female partner, or of a donor, known or stranger to all of them.

THERAPEUTIC CLONING: refers to cloning of an embryo for the purpose of deriving stem cells for therapeutic uses.

TISSUE OR CELL CULTURE: growth of tissue in a laboratory dish for experimental research.

TOTIPOTENT: refers to cells able to give rise to virtually any tissue type and in some cases to a functioning organism.

TRANSGENIC: having chromosomes into which one or more genes from different species have been incorporated either artificially or naturally.

ZONA: the thick protein shell which encases the ovum after ovulation occurs.

ZYGOTE: the earliest stage of human development from fertilization to the end of the second week.

ABOUT THE AUTHOR

Paul Szabo is the Member of Parliament for Mississauga South. He was first elected to the House of Commons in 1993 and was re-elected in 1997 and 2000 and he is currently the Parliamentary Secretary to the Minister of Public Works and Government Services. During his career, he has introduced over 20 Private Member Bills and Motions primarily on health and taxation issues related to children and families.

He also developed “Drink Smart Canada”, a national public education and awareness campaign on the misuse of alcohol and has authored six monographs: “Divorce - The Bold Facts”, “Strong Families Make a Strong Country”, “Tragic Tolerance of Domestic Violence”, “The Child Poverty Solution”, “Fetal Alcohol Syndrome – The Real Brain Drain”, and “The Ethics and Science of Stem Cells” all in support of his Private Member’s legislative initiatives.

A Chartered Accountant by profession, he also holds an M.B.A. from York University and a B.Sc. from the University of Western Ontario. Prior to his election, he worked in the corporate and public accounting sectors for over 23 years. Mr. Szabo’s extensive community service record also includes 9 years as a Director of the Mississauga Hospital, 5 years as a Director of Interim Place (community shelter for abused women and children), and 5 years as a Director of the Peel Regional Housing Authority.

Paul and his wife Linda have been married for 30 years and they have three grown children, Aaron, Reagan and Whitney.