WHEN DOES IT ALL BEGIN?

The embryo: of what importance; how sacred; and when does it become human?

by Gordon Giesbrecht, Ph.D.

I asked myself this question as I sat in my office preparing to testify before the House of Commons Standing Committee on Health regarding stem cell research. It was a daunting task, trying to convince this committee that they should include prohibition of research on embryonic stem cells in the government's proposed Bill C-13 (now C-6), An Act respecting human assisted reproduction and related research (passed and given Royal Assent on March 29, 2004).

What would I say? What was my position? Not wanting to risk spouting off rhetoric I had absorbed throughout a life of evangelical indoctrination, I started from scratch and got to the heart of the matter: when does human life begin? There is a vast diversity of opinion on this question. Several physical and time-based criteria are used to signify the start of life. What tipped the balance for me was more of a spiritual or metaphysical criterion; the acquisition of a soul. Although we do not often hear of this criterion, it should be considered since 83.5 per cent of Canadians identify with a religion that professes belief in a human soul. The definition of the start of human life is important since destruction of human embryos—and therefore human life—is central to the issue of stem cell research.

What are we talking about?

The discovery of stem cells has caused great excitement and expectations from physicians, researchers and the general public, especially in the past five years. These cells can differentiate into every type of body cell and tissue, making the potential for medical benefits enormous. Some current and proposed uses of stem cells include the possibilities of A) being isolated *in vitro* (outside the body) and manipulated to form new tissues for transplantation, B) being cultured *in vitro* for drug testing, and C) being implanted *in vivo* (in life) into traumatized or diseased areas of the body to replace defective or dying tissue. Seemingly, the sky is the limit and any disease can, theoretically, one day be cured.

At the heart of the ethical controversy over stem cell research is the source of stem cells themselves. Adult stem cells are derived from somatic (body) cells taken from various body tissues. Sources include skin, bone and even blood from the umbilical cord of newborns, and harvesting the cells does not harm the donor. On the other hand, embryonic stem cells are found in the human embryo and the harvesting process destroys the embryo. Thus the debate revolves around the moral status of the embryo and a corollary question, "When does human life begin?"

A basic overview may help the non-medical person get up to speed on this issue. The process of reproduction starts at conception (see Figure 1). Special reproductive cells, called gametes, are provided by the male (sperm) and female (egg). Each of these cells contains twenty-three chromosomes, which provide one half of the genetic material from each parent. Fertilization occurs when the sperm fuses with the egg, forming a zygote.

Zygote formation marks the beginning of a fascinating journey. This single cell is unique in that it contains the totality of human genetic information and is genetically unique from any other embryo. It has forty-six chromosomes and more than thirty thousand genes. This tiny cell has all the programming required for cell division, differentiation into various tissues and organs, biological system integration and production of human proteins and enzymes. Sex is determined and any genetic strengths and weaknesses are predetermined. All that is required for this single cell to develop through the embryonic (first eight weeks) and foetal (final seven months) phases of pregnancy to full-term birth is a suitable environment…and time!

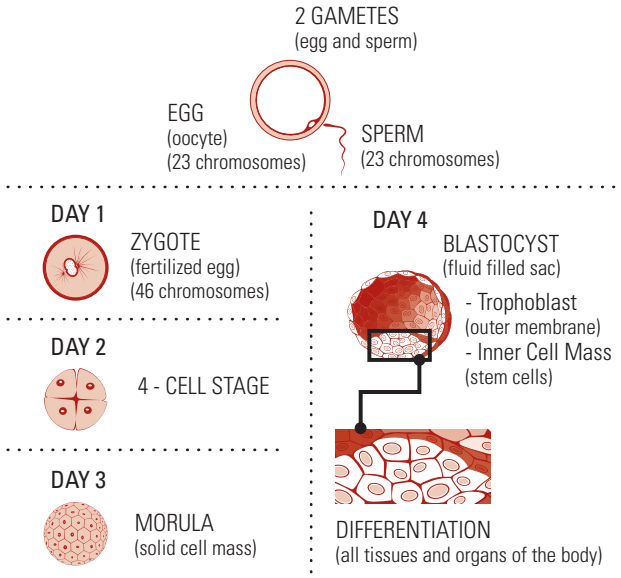

Figure 1

Essentially this single cell, through continued division and differentiation, forms the full human body. Differentiation is the process whereby dividing cells change to more and more specific types of cells. Each and every human cell has exactly the same genetic material. What is different is how the cell machinery implements different aspects of the genetic program to form different cell types. This is much like a complex computer program. Subroutines of the program may be used to create graphics, while different subroutines of the same program could be used to create a text document. In fact, thousands of different products can be produced by merely triggering different codes of the same program.

The embryo progresses through continued cell division to form a solid sphere of cells, the morula, by day three after fertilization. By day four, the cells then start to differentiate to form a fluid-filled sac, the blastocyst. The outer layer of the blastocyst, the trophoblast, is one-cell thick; these cells eventually differentiate further to form the placenta and amniotic tissue. Inside the blastocyst, an aggregation of a few dozen cells make up the inner cell mass (ICM). These ICM cells are stem cells in the earliest stage, which will eventually comprise every different type of tissue in the body. They first differentiate into three distinct germ layers.

Each layer further differentiates into a specific set of tissues–for instance the ectodermal layer differentiates to form skin cells and the nervous system, the mesodermal layer differentiates to form the musculoskeletal and cardiovascular systems and the endodermal layer differentiates to form several internal organs such as the lungs, liver, pancreas and intestines.

What's the big deal?

Two main ethical issues pervade the discussion of stem cell research: 1) the morality of destroying human embryos for research or disease treatment; and 2) the ethical implications of using cloning techniques to produce embryos for destruction.

Rights of the embryo

As stated above, adult stem cells are derived from body cells and harvesting them does not harm the donor. But harvesting embryonic stem cells does destroy the embryo. If you believe that life begins at conception, and the resultant embryo should be protected, you might ask, "Why not concentrate on adult stem cells and avoid the ethical debate?"

The drive to study embryonic stem cells emanates from the potentially greater 'potency'–the ability to differentiate into a larger range of tissues–than adult stem cells. Theoretically, during the first three days of development, cells progressing from the zygote to the morula are totipotent–they can become any cell type in the body. Blastocyst cells are pluripotent because they can form most but not all of the cell types. Trophoblast cells differentiate into the placenta and amniotic tissues, while only the inner cell mass cells can form all of the body cell types. Finally, cells in each of the three germ layers are multipotent and their differentiation is limited to specific types of cells (e.g. mammary stem cells can differentiate to form all the cells in a mammary gland).

As cells move toward more specific function, their potency–or ability to differentiate–diminishes and the scope of tissues that can be formed becomes more restricted. It is also believed that cells cannot move backwards and be coaxed into forming different cell types. It is this limitation that makes pluripotent embryonic stem cells more attractive to some researchers than adult stem cells, which are thought to be only multipotent. Although much of the research community, politicians and the public advocate this position, in actual fact adult stem cell research has been surprisingly successful.

Where does the embryo come from?

For a few decades, *in vitro* fertilization (IVF) clinics have helped many couples who were having problems achieving successful pregnancy. Essentially, IVF involves removing several eggs from a woman's ovary and initially freezing them. At some point, one or more of the eggs are thawed and introduced to sperm in a test tube, in the hopes that fertilization occurs. If successful, the embryo is incubated until a blastocyst is formed. After five or six days, the embryo is then introduced back into the uterus to implant itself in the uterus wall and, ideally, lead to a successful pregnancy. If and when this occurs, several other embryos may still remain in the frozen state. These 'left over' embryos have been a target source for embryonic stem cells (see Figure 2).

More recently, the term "cloning" has moved from science fiction to reality. Normally human cells have two sets of chromosomes (twenty-three from the father and twenty-three from the mother). A human clone is an embryo that has been manipulated such that both sets of chromosomes are from the same–living or deceased—human being, fetus or embryo. In other words, the cell essentially has the same genetic material as its single 'parent' cell.

There are different procedures and categories for cloning. Cloning can be accomplished by techniques such as parthenogenesis and embryo splitting and somatic cell nuclear transfer (see Figure 2). From an outcome perspective, reproductive cloning–which is almost universally condemned—involves nurturing a cloned embryo and implanting it in a woman's uterus in order to produce a cloned human baby. This sounds abhorrent, but several groups of scientists are actively pursuing this goal and several unsubstantiated announcements of successful clone-pregnancies have been made. Alternatively, therapeutic cloning involves the destruction of the cloned blastocyst in order to collect the inner cell mass for stem cell research.

The state of the art today

There is still a significant number of Canadians who feel that destroying embryos for research—whether they are 'left over' from IVF clinics, or are therapeutically cloned—is unacceptable because this process ends human life.

What are the actual results of this research? Despite the great furor in the press about the promise of embryonic stem cell (ESC) research, it is surprising to see the comparative progress on the

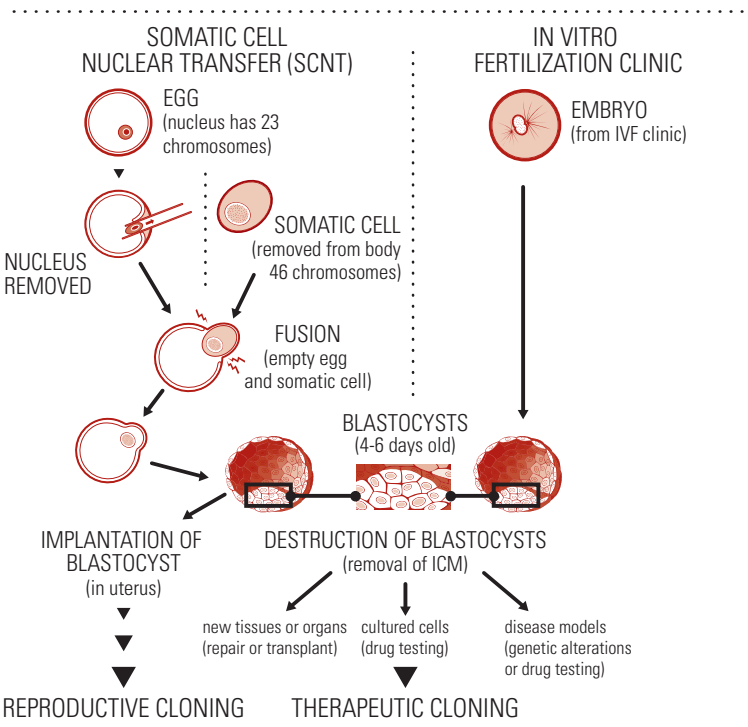

Figure 2 illustrates the somatic cell nuclear transfer (SCNT) method used for cloning an embryo. An egg has its nucleus removed. This nucleus contained the female donor's genetic material, but since the egg is a reproductive cell, it contains only half of the full genetic complement (or twenty-three chromosomes). A somatic, or body, cell (which contains a full compliment of genetic material, e.g. forty-six chromosomes) is removed from a human being, fetus or embryo. Normally a somatic cell–for instance a skin cell–cannot become anything different than what it already is. However, with SCNT, this cell is then fused with the empty egg. The resulting zygote essentially has the same genetic material as the donor and the egg provides an environment to sustain the life of the somatic cell nucleus which can now divide and create a blastocyst and a source for embryonic stem cells.

embryonic and adult stem cell fronts. In the United States, the Bush administration has limited funding for ESC, an event which may have focused more research on adult stem cells. In Canada, several other exciting studies have disproved the belief that adult stem cells have limited potency. For example, in British Columbia, stem cells have been isolated from breast tissue of mice that can regenerate an entire milk-producing mammary gland. Other research in Toronto has, for the first time, demonstrated stem cells in human skin that retained the ability to differentiate into neural, muscle and fat cells. The research shows that adult stem cells from several tissues in humans and/or other animals have properties of pluripotency. Thus, medical potential for adult stem cells seems impressive.

DoNoHarm: The Coalition of Americans for Research Ethics lists documented benefits of stem cell research to human patients. They state that sixty-five different diseases and injuries have been treated successfully with adult stem cells. A downloadable file lists 140 referred scientific publications in journals such as the New England Journal of Medicine and Lancet, that report successful treatments of cancer, autoimmune disease, immunodeficiencies, anemias, wound care and heart damage repair. It is difficult to find similar documented examples of successful treatments derived from embryonic stem cells.

Where do we go from here?

Whether or not embryonic stem cells provide medical advantages, one's own position on embryonic research should be based on a matter of principle: the moral status of the embryo itself. ESC research has been justified on the basis that at four to six days post-fertilization, the blastocyst is merely a clump of cells. Many authorities have set the threshold for human life at fourteen days post-fertilization. This period corresponds to two main events: 1) this is the approximate time when an embryo has completed its implantation in the uterus (it would not survive otherwise), and 2) the primitive streak usually starts to appear, which indicates the genesis of neural material.

Not only are these criteria not exact, there is another event that might be considered. When does the embryo receive its soul and begin its life? It is difficult to choose any time during gestation other than the point of conception itself. Based on this criterion, destruction of a blastocyst, no matter how small it may be, would be considered the ending of human life and therefore unethical.

I have noticed an interesting paradox related to this issue. Some strongly pro-life groups actually condone destructive embryonic research because of the potential medical advances. On the other hand, some pro-choice advocates actually oppose destructive embryonic research because the rights of the mother are not at issue.

When I testified before the Committee on Health in 2001, I found an unexpected ally. Maureen McTeer, a former commissioner on the Royal Commission on New Reproductive Technologies, and also the wife of former Prime Minister Joe Clark, caused a stir in the room when she advocated protection of embryos:

> *"There is a need to finally begin to recognize that these technologies force us all to rethink, and to do so outside of the context of the abortion debate, because there are two competing interests…in this case, where you deliberately create human life in vitro, you have the opportunity to in fact enlarge law's definitions to provide protection because it is human life…I wanted the principle to be clear: that what is threatening here is the notion of the human body being trivialized, the notion of human being trivialized."*

In North America more than 1.5 million abortions are performed annually. This death rate is fifty per cent higher than the Jewish holocaust of the Second World War, or alternatively be compared to 9/11 occurring every day. There is a new form of abortion infiltrating our medical research system today. If we believe that life begins at conception, then every set of embryonic stem cells harvested equates to an abortion. This is cause for alarm for many and should be an integral part of the debate surrounding stem cell research.

Canada's Bill C-6 prohibits creation of human embryos for research but under some circumstances does allow research on embryos created in IVF clinics for reproductive purposes but are no longer wanted. A study published in 2003 reported that 299 embryos from Canadian IVF clinics had been donated for research, representing two per cent of cryopreserved embryos. A subsequent study addressed whether IVF clinics adhered to Bill C-6 and rules set out by the Canadian Institutes of Health Research. Unfortunately only one of the fourteen IVF clinics responding to the survey, were operating in full accordance of the law. Thus, there is great potential for abuse of the system, and it may only get worse.

In conclusion, several things are clear. Embryonic stem cell research will be conducted throughout the world. Although most work is strictly controlled for medical treatment purposes now, more sinister uses like reproductive cloning and genetic engineering could become more prevalent. It is still worth continuing our own personal and national debate as we may eventually have to make decisions about using treatments derived from embryonic stem cell research. We still have to determine in our own minds at what stage an embryo is worthy of protection. We need to get the correct answer to the first question "Where does it all begin?" Only then will we be able to address the next question, "Where will it all end?"

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