Therapeutic vs. Reproductive Cloning: Scientific Realities, Public Controversy

When you hear the word “clone,” what images come to mind? Dolly, the first cloned mammal and probably the world’s most photographed sheep? The identical twins who live on your block? Or the endless lines of storm troopers in “Star Wars Episode II: Attack of the Clones”? Do you have trouble separating science fact from science fiction when it comes to cloning? If so, you are not alone!

Cloning has become a very controversial issue with scientists, lawmakers, religious leaders and the general public. The announcement of Dolly’s existence in February 1997 attracted enormous media interest, perhaps because it drew attention to the theoretical possibility of cloning humans. But very few scientists believe that human cloning should be permitted, and surveys show that most people disapprove of cloning designed solely to produce a human being (known as reproductive cloning).¹,²

On the other hand, many scientists are in favor of research into therapeutic cloning, which is the procedure used to produce embryonic stem cells that theoretically may be used to treat a number of diseases. Embryonic stem cells are the so-called starter cells that can turn into any sort of body tissue, from brain to bone to blood. These unspecialized cells also have the ability to divide for indefinite periods in tissue culture (in vitro). They are found in embryos during the early stages of development. Although the research is still in its infancy, scientists hope they will be able to use embryonic stem cells to generate specific tissues that can help repair damaged and diseased organs and provide alternatives to organ transplantation. Any disease in which cell death is a factor may be treatable in this way, and many of these illnesses — diabetes, heart disease, spinal cord injury, stroke, Alzheimer’s and Parkinson’s disease — have few or no treatment options.
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What is a Clone?
The word clone simply means “a precise genetic copy.” Scientists use this word as a shorthand term to refer to producing a copy of some biological entity — as simple as a piece of DNA or as complex as a plant or animal cell or even a whole organism.

Clones occur in nature all the time. In fact, humans have practiced cloning for thousands of years. Have you or someone in your family trimmed a houseplant and placed it in water to root? Once the roots appeared, did you place it in a new pot? If so, you produced a clone.

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>Number of Patients</th>
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<tr>
<td>Cardiovascular disease</td>
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<td>Autoimmune disease</td>
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<td>Alzheimer’s disease</td>
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<td>Parkinson’s disease</td>
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<td>Burns (severe)</td>
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<td>Spinal cord injuries</td>
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<td>Birth defects</td>
<td>0.15 million/year</td>
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The term cloning is confusing to the general public, however, because many people use it to mean lab techniques that created the sheep Dolly. That procedure is more correctly called somatic cell nuclear transfer (SCNT), and it works like this:

1. An unfertilized egg (an oocyte) from a female animal has its nucleus removed, creating an enucleated oocyte. The nucleus contains the cell’s chromosomes. Enucleation is accomplished by placing the egg under a microscope and illuminating it with ultraviolet light, which causes the genetic material to glow brightly. The egg is held in place with one pipette, and the genetic material is removed with another, sharp pipette. By removing the nucleus, the scientist eliminates the original genetic material.

2. The nucleus of a single somatic cell (any nonreproductive cell in the body) is then inserted into the enucleated oocyte. The somatic cell that donates the nucleus is usually one of many cells that have been removed from the animal to be cloned and grown in the laboratory using tissue culture. Dolly was created from a cultured mammary cell, and skin cells were also used.

3. The remaining reproductive “machinery” in the oocyte reprograms the genetic material of the somatic cell, producing a reconstituted embryo.

4. For reproductive cloning, the reconstituted embryo is placed into the uterus of a surrogate female. For human reproductive cloning, a female would donate her eggs to be enucleated. The nuclei of her cells would be removed and the person being cloned would donate somatic cells for the nuclear transfer. A surrogate mother would then accept the fertilized ova in hopes of carrying one egg to term.

5. For therapeutic cloning, the embryo is allowed to undergo cell division for several days in the laboratory until it reaches the blastocyst stage.
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A blastocyst consists of two layers: an outer layer of cells that goes on to form the placenta and other supporting tissues needed for development in the uterus and an inner mass that can form virtually all of the tissues of the body. To obtain embryonic stem cells, the blastocyst is opened, and the inner cell mass is placed in tissue culture. In culture, the cells divide and make exact copies of themselves, forming clones.

Obstacles to Reproductive Cloning Using Animals
The success rate for producing a live newborn animal using SCNT varies a lot among animal species, but this success rate is always very low — in many cases, three live births per 100 cloned embryos has been seen in many species (although the success rates continue to improve). The vast majority of problems occur during fetal development, and scientists are just beginning to investigate the reasons why. Fewer, but still significant, problems show up after birth — months or years later in the adult animals. Some cloned animals are developing physical problems at an earlier age than would be expected, some are becoming obese and some have unusual health problems. One significant problem at birth is called the “large offspring syndrome.” The cloned newborns are 20 to 30 percent larger than usual, making it hard for the pregnant animals to deliver such large babies. This problem appears to occur more often among ungulates (hoofed animals like sheep and cows) and rodents (mice and rats) than among primates.

Embryonic and Adult Stem Cells
To date, scientists have isolated two different types of stem cells: embryonic stem cells (which are also called pluripotent stem cells) and adult stem cells. (Note: Late-term fetuses and children have adult stem cells as well). Adult stem cells (also called multipotent stem cells) probably exist in very small numbers throughout the body, but the most accessible ones are the blood stem cells that reside in bone marrow. A brief course in embryology should help you understand the differences between the two types.

- The recently fertilized human egg is totipotent, meaning that its potential to become any type of cell is total. During the first rounds of cell division, each cell has the potential to form a fetus. Identical twinning can occur at this time — two totipotent cells separate and develop into two individual, genetically identical individuals. This type of “natural cloning” occurs for unknown reasons in about 3 of every 1,000 births.
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- After about four days and several rounds of cell division, these totipotent cells begin to specialize and form the blastocyst. The embryonic stem cells that constitute the inner mass of the blastocyst are described as being pluripotent. This means that they have the potential to become many types of cells, but no longer every type. In fact, if the inner cell mass was placed into a woman's uterus, it would not develop into a fetus.

As the fetus develops, the pluripotent stem cells undergo further specialization into adult stem cells. They are called multipotent because they are committed to give rise to more limited types of cells that have particular functions. For instance, skin stem cells give rise to various types of skin cells (like the different layers found in our outer skin), and blood stem cells give rise to red blood cells, white blood cells and platelets. Along with residing in the bone marrow of every child and adult, a small number of these cells can be found in the circulating blood and in the blood that remains in a newborn's umbilical cord after the baby is born. Parents of newborns now have the choice of banking their baby's umbilical cord blood in case the child needs new stem cells later in life. Scientists think the blood stem cells in umbilical cord blood may work better than those derived from bone marrow because they are less "mature."

Since new red blood cells, white blood cells and platelets are constantly being made throughout life, we couldn't survive without blood stem cells. For people whose blood stem cells have been destroyed by high-dose cancer chemotherapy or radiation therapy or have certain immune deficiency diseases, one treatment option is a bone marrow transplant. What they actually receive, however, is a transfusion of adult stem cells that have been isolated from a sample of bone marrow. In the case of patients with cancer, doctors freeze away some of the patients' own bone marrow before the treatment and give it back to them afterward. Patients with immune deficiency diseases, who may have defective or deficient numbers of blood stem cells, receive bone marrow from a well-matched relative or volunteer donor.
Therapeutic vs. Reproductive Cloning: Scientific Realities, Public Controversy (continued)

It is important to understand the differences between reproductive cloning, therapeutic cloning and stem cell research. The goal of reproductive cloning using SCNT is to create a new organism, human or animal. The goal of therapeutic cloning using SCNT is not to produce a new human being, which scientists agree is unsafe under present conditions, but to create embryonic stem cells that are genetically compatible with that of the recipient. Embryonic stem cells also can be isolated from embryos produced by the union of egg and sperm, but these stem cells will be genetically unique (like everyone’s, except identical twins’).

As a result of the confusion the two terms are generating, scientists are debating now about finding a better term for therapeutic cloning. One suggestion is “nuclear transplantation,” which captures the concept that the cell nucleus and genetic material are being moved from one cell to another.

Human Stem Cell Research

Human stem cell research faces heated opposition because it involves the use of human embryonic tissue. On Aug. 9, 2001, President George W. Bush made a significant decision regarding the funding of human stem cell research in the United States. He declared no federal funds would be used for: 1) the derivation or use of stem cell lines taken from newly destroyed embryos; 2) the creation of any human embryos for research purposes; and 3) the cloning of human embryos for any purpose. This decision did not affect research funded by private companies or state governments.

On March 9, 2009, President Barack Obama issued an executive order titled “Removing Barriers to Responsible Scientific Research Involving Human Stem Cells.” This order revoked President Bush’s 2001 decision and stated that the federal government can support and conduct responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by the law.
Scientists believe research with adult stem cells may eventually prove to be fruitful and negate the need for embryonic stem cell lines altogether. Although the research shows some promise, there are limitations to what may or may not be accomplished with adult stem cell lines:

- Right now, stem cells have not been isolated for all tissues of the body; missing ones include cardiac (heart) and pancreatic islet cells (the cells that produce insulin in the pancreas).
- Adult stem cells are often present in minute quantities and are difficult to isolate and purify. To minimize the chances of rejection, researchers would isolate the patient’s own stem cells and grow them in culture. For some diseases, there may not be enough time to grow them and use them for treatment.
- In disorders caused by a genetic defect, the genetic error would likely be present in the patient’s own stem cells. Even stem cells with no known genetic defect may contain DNA anomalies caused by a lifetime exposure to sunlight (UV radiation) and by toxins in our environment.
- There is evidence that stem cells from adults may not have the same ability to reproduce in culture as younger cells do.
- Adult stem cells do not seem to have the broad potential characteristics of the pluripotent embryonic stem cells. Studies of the early stages of cell specialization may not be possible with them.

The Therapeutic Potential of Stem Cells
Scientists point out that the creation of embryonic stem cells using SCNT does not really destroy embryos produced by the fusion of egg and sperm. This method instead uses an unfertilized egg with its nucleus removed and fuses it with the genetic material from an adult’s body. On the other hand, this fusion does have the potential to become a living thing, if transplanted into the uterus of a female. Is a life destroyed if you remove the stem cells from the blastocyst four days later? This is the question at the core of the debate about stem cell research.
The real advantage to producing stem cells via SCNT is that this process permits the production of perfect-match tissue. Theoretically, individuals with a disease could have stem cells produced that match their own cells, and these stem cells wouldn’t be seen as foreign and attacked by the individuals’ immune systems. Furthermore, these exact-match stem cells could become nerve cells, kidney cells, heart cells or whatever type of cell is needed to treat the disease.

Researchers have found that embryonic stem cells, when placed into various parts of the body, apparently want to “fit in” with their new neighbors. They pick up the developmental cues from their neighboring cells and differentiate into that cell type. Scientists believe this is the way stem cells will be used initially: individual stem cells will be implanted into the organ that needs repair, like the heart. Parkinson’s disease is one of many disorders that could benefit from cell therapy. It is a disorder of the nervous system that occurs when cells in a certain part of the brain stop producing a chemical called dopamine. Dopamine enables people to move normally and smoothly. By placing stem cells into that part of the brain, scientists hope these cells will differentiate and start producing dopamine. In fact, early animal experiments have found that this does occur. As our knowledge of stem cells advances, it may be possible to persuade stem cells to grow into complete organs — a possibility that is still many years away. Will this research lead to “miracle cures” or an “attack of the clones”? 