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Cloning: Where Do We Go From Here?

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Summary

News in February 1997 that scientists in Scotland had succeeded in cloning an adult sheep ignited a worldwide debate. Of concern are the ethical and social implications of the potential application of cloning to produce human beings. The announcement marked the first time that researchers were able to produce an exact genetic replica of an animal adult. Scientists identify a number of potential medical and agricultural applications for this technique. Within hours of the February 24 news, President Clinton asked his National Bioethics Advisory Commission (NBAC) to initiate a complete review of the ethical and social issues related to cloning and report back within 90 days. On March 4, 1997, the President sent a memorandum to the heads of all executive departments and agencies making it "absolutely clear that no federal funds will be used for human cloning." He also urged the private sector to adopt a voluntary ban on the cloning of humans until the NBAC completed its evaluation.

Bills were introduced in the 1st session that would ban federally supported human cloning research (S. 368 and H.R. 922), or human cloning altogether, H.R. 923 . One, H.R. 922, was reported to the House (amended), H.Rept. 105-239, but received no floor action. Hearings on cloning were held in both chambers. The NBAC presented its report in June, recommending — among other things — that federal legislation be enacted to prohibit anyone from attempting to create a child through cloning. The President sent up to Congress legislation (the "Cloning and Prohibition Act of 1997") reflecting the NBAC recommendations; however, it was not introduced in the first session. News reports on January 7, 1998, disclosed that a Chicago scientist, Dr. Richard Seed, intended to clone a human being and that he already had 8 volunteers who were willing to be cloned. Since then, 6 more cloning prohibition bills have been introduced: S. 1574, H.R. 3133, S. 1599, S. 1601, S.1602, and S.1611. On February 11, 1998, efforts to call up S.1601 for consideration in the Senate failed (by a vote of 42-54).

Background

On February 24, 1997, scientists at the Roslin Institute in Edinburgh, Scotland, announced that they had cloned an adult mammal for the first time. The researchers used

the nucleus of a mammary gland cell from an adult sheep and a sheep egg that had its nucleus removed. The two were fused using electrical pulses; the pulses also prompted the egg to start dividing and form an embryo. The embryo was then transferred to the uterus of a surrogate sheep, where, one embryo implanted and grew to term resulting in the birth of a live lamb, Dolly.[1] Analyses of the genetic material confirmed that Dolly was derived from the adult lamb's mammary cell. Before cloning the adult sheep, scientists believed that an early embryo was required as the source of the genetic material for cloning and that a clone could not be derived from a cell of an adult animal.

The cloning method used to produce Dolly, known as somatic cell nuclear transfer cloning, could have a number of significant medical and agriculture applications. Examples include the creation of improved breeds of livestock, development of animals that can produce drugs for use by or whose organs can be used in, humans. In the sheep cloning experiment, the number of embryo implants that resulted in live births was very low. A total of 277 fused eggs were implanted, but only one lamb was born. However, researchers believe that further research will improve the efficiency of the technique. It does not yet appear possible to clone humans. Nevertheless, a major concern of many people, including some who support the cloning of animals, is that this technique could in the future be developed to a point that would make it possible to clone humans.

In response to concerns about the potential application of cloning to produce humans, actions were taken by the Administration and Congress. President Clinton, on February 24, 1997, asked the NBAC[2] to thoroughly review the ethical and legal issues associated with the use of cloning technology. The Commission reported its findings and recommendations to the President on June 9, 1997. It recommended that federal legislation be enacted to prohibit the use of cloning to create a child in both the public and private sector. The NBAC found it morally unacceptable at this time to attempt to clone humans because current scientific data indicate that the method is not safe. The "Cloning and Prohibition Act" which the President sent to Congress for "immediate consideration and prompt enactment" was not introduced in the first session of 105th Congress. However, several bills which would ban cloning were introduced.

Legislation was introduced in the Senate on February 27, 1997, and House on March 5, 1997, that would prohibit the use of federal funds for human cloning research (S. 368 and H.R. 922), or, human cloning altogether (H.R. 923). H.R. 922, the Human Cloning Research Prohibition Act, would prohibit the use of federal funds for any cloning research, including the use of human somatic cell nuclear transfer technology to produce an embryo. The bill would allow federal funds to be used to support research involving somatic cell nuclear transfer or other cloning techniques to clone molecules, DNA cells other than human embryo cells, or tissue. The use of somatic cell nuclear techniques to create nonhuman animals would be permitted. H.R. 922 was reported to the House from the Committee on Science (amended) on August 1, 1997 (H.Rept. 105-239, Part I).

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[1] Wilmut, I. et.al. Viable Offspring Derived From Fetal and Adult Mammalian Cells. Nature, v.385, February 27, 1997, pp. 810-813.

[2] NBAC was established by Presidential Executive Order 12975 on October 3, 1995, to provide guidance to federal agencies on the ethical conduct of current and future human biological and behavioral research.

A number of cloning prohibition bills have been introduced in the second session. S. 1574 (Campbell), the "Human Cloning Prohibition Act," introduced on January 27, 1998, would prohibit the cloning of a human being or research for the purpose of cloning a human being or otherwise creating a human embryo. H.R. 3133 (Stearns), the "Human Cloning Research Prohibition Act," introduced on January 28, 1998, would prohibit federal funding of research that includes the use of human somatic cell nuclear transfer technology to produce an oocyte that is undergoing cell division toward development of a fetus. S. 1599 (Bond) and S. 1601 (Lott), the "Human Cloning Prohibition Act of 1998," introduced on February 3, 1998, would prohibit the use of, and the importation of, an embryo produced through human somatic cell nuclear transfer technology. S. 1602/S.1611 (Feinstein), the "Prohibition on Cloning of Human Beings Act of 1998," introduced on February 3, 1998 and February 4, 1998, respectively, would prohibit the implantation or attempt to implant the product of somatic cell nuclear transfer into a woman's uterus."

What Is Cloning? Cloning is defined as making genetically identical copies of a single cell or organism.[3] Before cloning the adult sheep, researchers had created animal clones only from early embryos, or embryo-derived cells. Cloning of animals has been done using one of three techniques: blastomere separation, blastocyst division and twinning, or nuclear transplantation. For each technique, an embryo is produced by in vitro fertilization (IVF), where an egg is fertilized with sperm in a laboratory dish. Once fertilized, the embryo is allowed to divide into a 2- to 8-cell stage and then is cloned by one of the three techniques.[4]

In Blastomere Separation,[5] the outer coating, or zona pellucida, is removed from around a 2- to 8-cell embryo, then placed in a special solution that causes the cells, called blastomeres, to separate. Each cell can then be cultured individually, because at this stage of embryo development, each cell is totipotent, that is, it is undifferentiated and can develop into an organism. After dividing a few times, each blastomere may develop into a smaller-than-normal embryo that can be transferred to the uterus.

In Blastocyst Division, also called ***induced twinning***, an embryo, at the blastocyst stage, a more advanced stage of development than the blastomere, is mechanically split into two. The two parts can be transferred to the uterus. If both halves develop, then, at most, one blastocyst gives rise to identical twins.

In Nuclear Transplantation, a nucleus is transferred from each blastomere of a 4- to 8-cell or later-stage embryo into the cytoplasm (cell contents other than nucleus) of an egg from which the genetic material has been removed (enucleated egg). To do this, the blastomere is placed beside an enucleated egg and their membranes are fused together

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[3] National Institutes of Health. Report of the Human Embryo Research Panel, vol. 1, September 1994, p. D-4.

[4] Today, in treating infertile couples, once an embryo is created by IVF, it is allowed to divide into a 32-cell stage embryo and can then be transferred to the patient's uterus. If the procedure is successful, the embryo implants and results in the birth of a baby.

[5] The information describing the 3 cloning techniques was obtained from The NIH Report of the Human Embryo Research Panel, September 1994.

artificially for example, with electrical pulses. The nucleus from the blastomere enters the egg cytoplasm and directs development of the embryo.

The Scottish scientists used a variant of the nuclear transplantation technique, where the nucleus that programmed the creation of Dolly was transferred from the **adult** sheep mammary cell, not an **embryo**. Researchers had thought that when cells became differentiated to do certain jobs in the body, they could not revert to the embryo stage. For example, they thought that a cell that became a liver cell remained a liver, but that belief was disproved by the Scottish scientists. They were able to reprogram the genes in a mammary-gland cell to make it act like an undifferentiated embryo, which then developed into a sheep.

Potential Uses of Cloning

Cloning conceivably could be used to produce large numbers of genetically identical organisms. However, many scientists wish to use it as a research tool to understand how genes in cells can be switched off and on. Each cell in the body (with a few exceptions) has the same genes. One embryo cell becomes mammary tissue and another liver when certain genes are switched on and others switched off. The technique used by the Scottish scientists turned off the genes for mammary function and turned on those that function at the embryo stage. But scientists do not know how the technique worked. When more is known, the hope is that this knowledge can be used for other research, such as growing new skin for burn victims, culturing bone marrow that could be used to treat cancer patients, and manipulating genes to cure sickle cell anemia.

The first public report of cloning human embryos occurred in 1993.[6] However, those embryos were never transferred into the uterus. Using IVF embryos which were determined to be unsuitable to be transferred to the uterus, researchers at an IVF clinic at George Washington University (GWU), supported with private funds, cloned the early human embryos with the blastomere separation method. Seventeen 2- to 8-cell embryos, which had been fertilized in vitro were separated into individual blastomeres and placed in a special solution so that they could divide again. A total of 48 new embryos were produced, although, most of them did not develop to the stage where they could be implanted into the uterus (32-cell stage).

One potential application of cloning human embryos may be to treat infertility. Infertility affects more than 2.8 million U.S. couples. About one-half of those couples eventually conceive with some form of treatment, such as IVF. There have been more than 16,000 IVF births worldwide since 1978 when the first IVF birth, of Louise Brown, occurred in England. However, the overall live-birth rate for IVF is low. Research indicates that if more than one embryo is transferred to the uterus per treatment cycle, the chance that at least one will implant and lead to a live birth increases. However, some patients (for example, older reproductive-age and so-called “poor responder” patients) undergoing IVF have a limited number of embryos for transfer and implantation. Researchers have suggested that those patients could benefit from having their embryos

[6] Kolberg, R. Human Embryo Cloning Reported. Sci.,v. 262, Oct. 29, 1993, p. 652-653.

cloned. However, it is unclear that embryo cloning would help in these cases because the quality of the embryos from such patients also tends to be diminished.[7]

An application of blastomere separation that is being done in the private sector and is known as preimplantation diagnosis may be improved with cloning research. This technique has been used experimentally to diagnose an early embryo for diseases like cystic fibrosis, Duchenne muscular dystrophy, and Tay-Sachs. In the procedure, one or two cells can be removed from an IVF embryo at the 8- to 16-cell stage for biopsy, without affecting subsequent development of the embryo. The genetic material retrieved for biopsy is analyzed for the presence or absence of a specific genetic defect. Unaffected embryos can then be transferred to a woman's uterus for implantation on the same day as the biopsy. Since 1992 when this experimental technique was first used, more than 30 healthy children have been born worldwide as a result of preimplantation diagnosis.

Ethical and Social Issues

The possibility of cloning human beings raises profound moral and ethical questions. No scientific rationale has yet been identified for cloning an existing human. NIH Director Harold Varmus stated at a February 26, 1997 hearing held by the House Appropriations Subcommittee on Labor, HHS, and Education that he personally agrees with the public's opinion that cloning human beings is "repugnant." A major concern is that cloning would seriously affect society's perception of what it means to be a human being. There are also unanswered questions about a cloned individual's personal identity, uniqueness, and individuality. Many worry that cloning would lead to diminished respect for humans in general, and for cloned individuals, in particular, since the cloned person could simply be replaced with another clone. Others point out, that does not occur today with identical twins, who are naturally produced clones.

In addition to possible problems related to individuality, identity, and human values, cloning human embryos raises difficult questions about the rights of parents to control their own embryos, other issues in reproductive rights, and privacy. Some observers believe that it would be ethical to clone human embryos to help infertile couples conceive in an IVF setting. For example, some believe that the technique, if perfected, could be used by parents to grow one embryo to term and store (by freezing) the others indefinitely. Later, one of these spare embryos could be thawed, transferred, implanted, and grown to term, where it would become an identical, but younger, twin of the first sibling. Many are concerned, however, that the production of a human clone of an existing embryo would be counter to human values as civilization has defined them. Some parents might want to store embryo clones as a backup in case their child died, or so that if their child needed an organ or tissue transplant, such as bone marrow, the mother could give birth to the child's identical twin. Others argue that the use of clones as potential sources of tissue or organs would be unethical. The National Advisory Board on Ethics in Reproduction (NABER) has recommended that legislation be enacted to ban the commercial use of human embryos.[8]

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[7] Jones, H.W. et.al. On Attempts at Cloning in the Human. Fertility and Sterility vol. 61, March 1994, pp. 423-426.

[8] National Advisory Board on Ethics in Reproduction. Report on Human Cloning through (continued...)

Regulation/Guidelines

Currently no regulations exist in the United States that would prohibit cloning research like that done in Scotland, in which cells from an adult animal were used to make the sheep clone. However, restrictions have been in place since January 1996 that prohibit the Department of Health and Human Services (DHHS) from using federal funds to support cloning research involving human embryos[9] (see CRS Report 95-910). President Clinton's March 4 directive to all executive departments and agencies extends this ban to all federally supported research, but does not apply to research done in the private sector.

An NIH-appointed Human Embryo Research Panel in 1994 developed guidelines and recommendations on human embryo research. It determined that cloning by blastomere separation or blastocyst splitting without transfer to the uterus warranted additional review before the Panel could recommend whether the research should be federally funded. However, the Panel concluded that federal funding for cloning by these two techniques followed by transfer to the uterus should be unacceptable into the foreseeable future. NIH's review in this area was halted with the 1996 DHHS appropriations ban and a similar ban applies to FY1998 funds (see CRS Report 95-910 for more information on the human embryo research ban).

In the United States, human IVF has been developed and advanced in the private sector. Currently, more than 300 IVF clinics are located throughout the United States and operate with no federal money and little federal oversight. A law enacted in 1992, P.L. 102-493, mandates that all assisted reproductive technology programs comply with certification and pregnancy-success-rates reporting-requirements. The Centers for Disease Control and Prevention of the DHHS is responsible for implementing the Fertility Clinic Success Rate and Certification Act of 1992. CDC released its first set of reports that rate the success of more than 280 fertility clinics in the United States.[10] Guidelines have been developed by the industry but compliance is voluntary.

The American Society for Reproductive Medicine, which represents most of the IVF clinics, published a set of ethical considerations for assisted reproductive technologies in 1994 for its members. Included was a recommendation that human blastomere research be performed to determine which, if any, clinical indications may justify the practical use of this technology. Guidelines on human cloning through blastomere separation were developed by NABER in 1994. The group opposed certain applications of cloning, including that done only to produce identical twins separated by years.

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[8](...continued)
Embryo Splitting: An Amber Light.Kennedy Institute of Ethics Journal, Vol. 4, September 1994, pp. 251-282.

[9] The National Institutes of Health (NIH), the agency that might support human embryo research was prohibited from using FY1996 appropriated funds to support human embryo research including that involving cloning with the January 26, 1996 enactment of P.L.104-99. This restriction also applied to NIH FY1997 appropriations, P.L.104-208 and applies to NIH FY1998 appropriations, P.L.105-78.

[10] 1995 Assisted Reproductive Technology Success Rates. National Summary and Fertility Clinic Reports, Volumes I, II, III, Centers for Disease Control and Prevention, American Society for Reproductive Medicine, and Resolve, December 1997.