

To: ELIZABETH DRYE

FROM: DR. HAROLD T. SHAPIRO

6 PAGES (INCL. COVER)



EXECUTIVE SUMMARY

The idea that humans might someday be cloned—created from a single somatic cell without sexual reproduction—moved further away from science fiction and closer to a genuine scientific possibility on February 23, 1997. On that date, *The Observer* broke the news that Ian Wilmut, a Scottish scientist, and his colleagues at the Roslin Institute were about to announce the successful cloning of a sheep by a new technique which had never before been fully successful in mammals. The technique involved transplanting the genetic material of an adult sheep, apparently obtained from a differentiated somatic cell, into an egg from which the nucleus had been removed. The resulting birth of the sheep, named Dolly, on July 5, 1996, was different from prior attempts to create identical offspring since Dolly contained the genetic material of only one parent, and was, therefore, a "delayed" genetic twin of a single adult sheep.

This cloning technique is an extension of research that had been ongoing for over 40 years using nuclei derived from non-human embryonic and fetal cells. The demonstration that nuclei from cells derived from an adult animal could be "reprogrammed," or that the full genetic complement of such a cell could be reactivated well into the chronological life of the cell, is what sets the results of this experiment apart from prior work. In this report we refer to the technique, first reported by Wilmut, of nuclear transplantation using nuclei derived from somatic cells other than those of an embryo or fetus as "somatic cell nuclear transfer."

Within days of the published report of Dolly, President Clinton instituted a ban on federal funding related to attempts to clone human beings in this manner. In addition, the President asked the recently appointed National Bioethics Advisory Commission (NBAC) to address within ninety days the ethical and legal issues that surround the subject of cloning human beings. This provided a welcome opportunity for initiating a thoughtful analysis of the many dimensions of the issue, including a careful consideration of the potential risks and benefits. It also presented an occasion to review the current legal status of cloning and the potential constitutional challenges that might be raised if new legislation were enacted to restrict the creation of a child through somatic cell nuclear transfer cloning.

The Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo, with the apparent potential to be implanted in utero and developed to term. Ethical concerns surrounding issues of embryo research have recently received extensive analysis and deliberation in our country. Indeed, federal funding for human embryo research is severely restricted, although there are few restrictions on human embryo research carried out in the private sector. Thus, under current law, the use of somatic cell nuclear transfer to create an embryo solely for research purposes is already restricted in cases involving federal funds. There are, however, no current federal regulations on the use of private funds for this purpose.

The unique prospect, vividly raised by Dolly, is the creation of a new individual

genetically identical to an existing (or previously existing) individual—a “delayed” genetic twin. This prospect has been the source of the overwhelming public concern about such cloning. The Commission recognizes that any creation of embryos for research purposes alone raises serious ethical issues. However, these ethical issues have already been extensively discussed, and the use of somatic cell nuclear transfer to create embryos raises no new issues in this respect. The unique and distinctive ethical issues raised by the use of somatic cell nuclear transfer to create children relate to, for example, serious safety concerns, individuality, family integrity, and treating children as objects. Consequently, the Commission focused its attention on the use of such techniques for the purpose of creating an embryo which would then be implanted in a woman's uterus and brought to term. It also expanded its analysis of this issue to encompass activities in both the public and private sector.

In its deliberations, NBAC reviewed the scientific developments which preceded the Roslin announcement, as well as those likely to follow in its path. It also considered the many moral concerns raised by the possibility that this technique could be used to clone human beings. Much of the initial reaction to this possibility was negative. Careful assessment of that response revealed fears about harms to the children who may be created in this manner, particularly psychological harms associated with a possibly diminished sense of individuality and personal autonomy. Others expressed concern about a degradation in the quality of parenting and family life.

In addition to concerns about specific harms to children, people have frequently expressed fears that a widespread practice of somatic cell nuclear transfer cloning would undermine important social values by opening the door to a form of eugenics or by tempting some to manipulate others as if they were objects instead of persons. Arrayed against these concerns are other important social values, such as protecting the widest possible sphere of personal choice, particularly in matters pertaining to procreation and child rearing, maintaining privacy, and the freedom of scientific inquiry, and encouraging the possible development of new biomedical breakthroughs.

To arrive at its recommendations concerning the use of somatic cell nuclear transfer techniques to create children, NBAC also examined long-standing religious traditions that guide many citizens' responses to new technologies and found that religious positions on human cloning are pluralistic in their premises, modes of argument, and conclusions about human cloning. Some religious thinkers argue that the use of somatic cell nuclear transfer cloning to create a child would be intrinsically immoral and thus could never be morally justified. Other religious thinkers contend that human cloning to create a child could be morally justified under some circumstances, but hold that it should be strictly regulated in order to prevent abuses.

The public policies recommended with respect to the creation of a child using somatic cell nuclear transfer reflect the Commission's best judgments about both the ethics of attempting such an experiment and our view of traditions regarding limitations on individual actions in the name of the common good. At present, the use of this technique to create a child would be a

premature experiment that would expose the fetus and the developing child to unacceptable risks. This in itself is sufficient to justify a prohibition on cloning human beings at this time, even if such efforts were to be characterized as the exercise of a fundamental right to attempt to procreate.

Beyond the issue of the safety of the procedure, however, NBAC found that concerns relating to the potential psychological harms to children and effects on the moral, religious, and cultural values of society merited further reflection and deliberation. Whether upon such further deliberation our nation will conclude that the use of cloning techniques to create children should be allowed or permanently banned is, for the moment, an open question. Time is an ally in this regard, allowing for the accrual of further data from animal experimentation, enabling an assessment of the prospective safety and efficacy of the procedure in humans, as well as granting a period of fuller national debate on ethical and social concerns. The Commission therefore concluded that there should be imposed a period of time in which no attempt is made to create a child using somatic cell nuclear transfer.¹

Within this overall framework the Commission came to the following conclusions and recommendations.

I. The Commission concludes that at this time it is morally unacceptable for anyone in the public or private sector, whether in a research or clinical setting, to attempt to create a child using somatic cell nuclear transfer cloning. We have reached a consensus on this point because of insufficient information on the safety and effectiveness of this method in humans. Indeed, we believe it would violate important ethical obligations were clinicians or researchers to attempt to create a child using these particular technologies, which are likely to involve substantial risks to the fetus and/or potential child. Moreover, in addition to safety concerns, many other serious ethical concerns have been identified, which require much more widespread and careful public deliberation before this technology may be used.

The Commission, therefore, recommends the following for immediate action:

- A continuation of the current moratorium on the use of federal funding in support of any attempt to create a child by somatic cell nuclear transfer.
- An immediate request to all firms, clinicians, investigators, and professional societies in the private and non-federally funded sectors to comply voluntarily with the intent of the federal moratorium. Professional and scientific societies should make clear that any attempt to create a child by somatic cell nuclear transfer and implantation into a woman's

¹ The Commission also observes that the use of any other technique to create a child genetically identical to an existing (or previously existing) individual would raise many, if not all, of the same non-safety-related ethical concerns raised by the creation of a child by somatic cell nuclear transfer.

body would at this time be an irresponsible, unethical, and unprofessional act.

II. The Commission further recommends that:

- Federal legislation should be enacted to prohibit anyone from attempting, whether in a research or clinical setting, to create a child through somatic cell nuclear transfer cloning. It is critical, however, that such legislation include a sunset clause to ensure that Congress will review the issue after a specified time period (three to five years) in order to decide whether the prohibition continues to be needed. If state legislation is enacted, it should also contain such a sunset provision. Any such legislation or associated regulation also ought to require that at some point prior to the expiration of the sunset period, an appropriate oversight body will evaluate and report on the current status of somatic cell nuclear transfer technology and on the ethical and social issues that its potential use to create human beings would raise in light of public understandings at that time.

III. The Commission also concludes that:

- Any regulatory or legislative actions undertaken to effect the foregoing prohibition on creating a child by somatic cell nuclear transfer should be carefully written so as not to interfere with other important areas of scientific research. In particular, no new regulations are required regarding the cloning of human DNA sequences and cell lines, since neither activity raises the scientific and ethical issues that arise from the attempt to create children through somatic cell nuclear transfer, and these fields of research have already provided important scientific and biomedical advances. Likewise, research on cloning animals by somatic cell nuclear transfer does not raise the issues implicated in attempting to use this technique for human cloning, and its continuation should only be subject to existing regulations regarding the humane use of animals and review by institution-based animal protection committees.
- If a legislative ban is not enacted, or if a legislative ban is ever lifted, clinical use of somatic cell nuclear transfer technique to create a child should be preceded by research trials that are governed by the twin protections of independent review and informed consent, consistent with existing norms of human subjects protection.
- The United States Government should cooperate with other nations and international organizations to enforce any common aspects of their respective policies on the cloning of human beings.

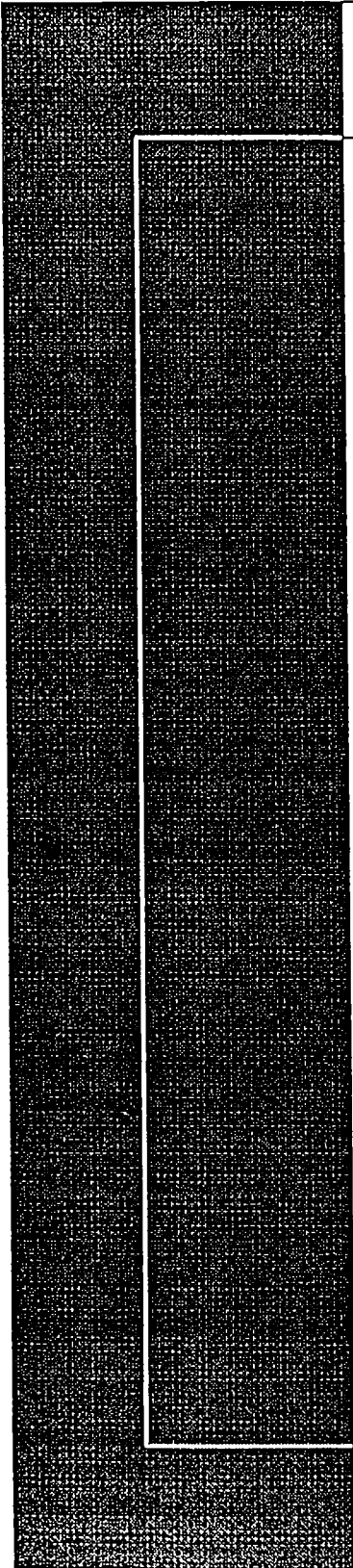
IV. The Commission also concludes that different ethical and religious perspectives and traditions are divided on many of the important moral issues that surround any attempt to create a child using somatic cell nuclear transfer techniques. Therefore, we recommend that:

- The federal government, and all interested and concerned parties, encourage widespread

and continuing deliberation on these issues in order to further our understanding of the ethical and social implications of this technology and to enable society to produce appropriate long-term policies regarding this technology should the time come when present concerns about safety have been addressed.

V. Finally, because scientific knowledge is essential for all citizens to participate in a full and informed fashion in the governance of our complex society, the Commission recommends that:

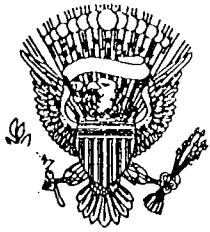
- Federal departments and agencies concerned with science should cooperate in seeking out and supporting opportunities to provide information and education to the public in the area of genetics, and on other developments in the biomedical sciences, especially where these affect important cultural practices, values, and beliefs.



CLONING HUMAN BEINGS

Report and Recommendations of the
National Bioethics Advisory Commission

Rockville, Maryland
June 1997



National Bioethics Advisory Commission

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June 6, 1997

Dear President Clinton:

On February 24, 1997, in the wake of the announcement that scientists in Scotland apparently had succeeded in cloning an adult sheep, you asked the National Bioethics Advisory Commission to review the legal and ethical issues associated with the use of this technology and to report back within ninety days with recommendations. A week later you instructed the heads of executive departments and agencies that "no federal funds shall be allocated for cloning of human beings" thereby ensuring that precipitous steps would not be taken while the Commission was studying the subject.

In this short interval, we have made every effort to consult with ethicists, theologians, scientists, physicians, and other citizens with interests and concerns in this area. Moreover, we have invited inputs for the Commission's consideration from as broad a cross-section of the community as time allowed. Further, recognizing that science and medicine are international activities with outstanding investigators and facilities in many nations, we have attempted to review relevant policies and proposals with respect to human cloning in other countries. However, we do not view it as essential to follow others in this area unless we find their proposals compelling, since we have different political and cultural traditions.

In this report, we address a very specific aspect of cloning namely where genetic material would be transferred from the nucleus of a somatic cell of an existing human being to an enucleated human egg with the intention of creating a child. The cloning of humans by embryo-splitting is not examined.

Not surprisingly, we have discovered that the potential ability to clone human beings through the somatic cell nuclear transfer techniques raises a whole host of complex and difficult scientific, religious, legal and ethical issues--both new and old. Indeed, the Commission itself is unable to agree at this time on all the ethical issues that surround the issue of cloning human beings in this manner. It seems clear to all of us, however, given the current stage of science in this area, that any attempt to clone human beings via somatic cell nuclear transfer techniques is uncertain in its prospects, is unacceptably dangerous to the fetus and, therefore, morally unacceptable. At present, moral consensus on this issue should be easily achieved. We therefore recommend that the current moratorium on attempts to create children in this manner be continued and that you immediately ask for voluntary compliance in the private sector while federal legislation banning the use of these techniques for creating children is formulated and considered.

While we have been able to agree on this and certain other recommended actions, we feel quite strongly that most of the legal and moral issues raised can only be resolved, even temporarily, by a great deal more widespread deliberation and education. This type of national discussion is especially necessary in our pluralistic society for the following reasons: there is no universally accepted ethical theory; Americans hold various religious and moral perspectives on these issues; conflicting values are at stake; Americans differ on the importance and meaning of particular traditions; tolerance (agreeing to disagree) governs wide areas of our national life; and given our historical traditions, we are strongly inclined to leave to the individual conscience those acts that do not harm others and on which there is no moral consensus.

As a result, while our specific recommendations include continuing the moratorium you announced in February of this year, and a call for a specific federal legislation, the report also includes important sections outlining the scientific, religious, ethical and legal issues that are raised by these new scientific developments. It is our hope that these materials, by clarifying certain issues and highlighting others, will form a useful initial basis for the ongoing deliberations and educational dialogues that we believe are so essential. We have been impressed by the difficulties caused by the lack of knowledge about genetics and the science involved in cloning revealed in the public and media responses to the cloning of Dolly the sheep. We believe, therefore, that the federal government should continue to actively encourage public education in this area of science so that as public deliberation takes place it is as informed as possible.

Finally, we must continue to build our understanding of the widespread public concern that has been generated by these recent developments. Some of this concern can be explained by an inadequate understanding of the issues--sometimes even confusing science and science fiction. This matter, however, can be addressed over time through further public education. Other concerns, however, run much deeper and range from the implications for particular faith commitments, to views regarding the appropriate sphere for human action, to concerns regarding the future of the family, to cumulative apprehensions about the real net benefit of a rapidly advancing technology that some believe is too aggressively pushing aside important social and moral values. As we move ahead to the next stage of our national discussion, these are among the many issues that need to be thoughtfully addressed.

I would like to take this opportunity to thank all the Commissioners and our very dedicated staff for the intensity and depth of their commitment to the task that you assigned to us.

Sincerely,

Harold T. Shapiro

THE WHITE HOUSE
WASHINGTON

February 24, 1997

Dr. Harold Shapiro
Chair
National Bioethics
Advisory Commission
Suite 3C01
6100 Executive Boulevard
Bethesda, Maryland 20892-7508

Dear Dr. Shapiro:

As you know, it was reported today that researchers have developed techniques to clone sheep. This represents a remarkable scientific discovery, but one that raises important questions. While this technological advance could offer potential benefits in such areas as medical research and agriculture, it also raises serious ethical questions, particularly with respect to the possible use of this technology to clone human embryos.

Therefore, I request that the National Bioethics Advisory Commission undertake a thorough review of the legal and ethical issues associated with the use of this technology, and report back to me within ninety days with recommendations on possible federal actions to prevent its abuse.

Sincerely,

A handwritten signature in black ink, appearing to read "Bill Clinton", with a long horizontal flourish extending to the right.

National Bioethics Advisory Commission

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The Commission wishes to thank Dr. Kathi Hanna, Ms. Henrietta Hyatt-Knorr, and the NBAC staff for their unfailing commitment throughout the 90 days in which this report was formulated and produced. Others who provided superior support include Dr. William Raub, Ms. Lili Engstrom, Mr. Hal Thompson, Mr. Damon Thompson, Ms. Donna Young, Mr. Timothy Morris, Mr. Vito Oporto, Ms. Janet Miller, and Ms. Marcia Snowden.

EXECUTIVE SUMMARY

[by splitting the blastomere]

The idea that humans might someday be cloned—created from a single somatic cell without sexual reproduction—moved further away from science fiction and closer to a genuine scientific possibility on February 23, 1997. On that date, *The Observer* broke the news that Ian Wilmut, a Scottish scientist, and his colleagues at the Roslin Institute were about to announce the successful cloning of a sheep by a new technique which had never before been fully successful in mammals.

The technique involved transplanting the genetic material of an adult sheep, apparently obtained from a ~~fully differentiated somatic cell~~ ^{non-embryonic}, into an egg from which the nucleus had been removed. STET

The resulting birth of the sheep, named Dolly, on July 5, 1996, was different from prior attempts to create identical offspring from a pair of adult animals since Dolly contained the genetic material of only one parent, and was, therefore, a "delayed" genetic twin of a single adult sheep.

This cloning technique, ~~referred to in this report as "somatic cell nuclear transfer,"~~ is an extension of research that had been ongoing for over 40 years. The demonstration that a somatic cell's gene expression could be "reprogrammed," or that the full genetic complement of the cell could be reactivated well into the chronological life of the cell, is what sets the results of this experiment apart from prior work. *on this report we refer to*

this technique first reported by Wilmut, using a non-embryonic somatic cell — non-embryonic somatic cell nuclear transfer.

Within days of the published report of Dolly, President Clinton instituted a ban on federal funding related to attempts to clone human beings in this manner. In addition, the President asked the recently appointed National Bioethics Advisory Commission (NBAC) to address within ninety days the ethical and legal issues that surround the subject of cloning human beings. This provided a welcome opportunity for initiating a thoughtful analysis of the many dimensions of the issue, including a careful consideration of the potential risks and benefits. It also presented an occasion to review the current legal status of cloning and the potential constitutional challenges that might be raised if new legislation were enacted to restrict the creation of a child through somatic cell nuclear transfer cloning.

The Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo, with the apparent potential to be implanted in utero and developed to term. Ethical concerns surrounding issues of embryo research have recently received extensive analysis and deliberation in our country. Indeed, federal funding for human embryo research is severely restricted, although there are few restrictions on human embryo research carried out in the private sector. Thus, under current law, the use of somatic cell nuclear transfer to create an embryo solely for research purposes is already restricted in cases involving federal funds. There are, however, no current federal regulations on the use of private funds for this purpose. NBAC did not review these particular issues in the context of this report. Instead, it focused its attention on the use of such techniques for the purpose of creating an embryo which would then be implanted in a woman's uterus and brought to term. It also expanded its analysis of this issue to encompass activities in both the public and private sector.

1 In its deliberations, NBAC reviewed the scientific developments which preceded the
2 Roslin announcement, as well as those likely to follow in its path. It also considered the many
3 moral concerns raised by the possibility that this technique could be used to clone human beings.
4 Much of the initial reaction to this possibility was negative. Careful assessment of that response
5 revealed fears about harms to the children who may be created in this manner, particularly
6 psychological harms associated with a possibly diminished sense of individuality and personal
7 autonomy. Others expressed concern about a degradation in the quality of parenting and family
8 life if a child's development was no longer fully unpredictable, especially if parents were to
9 confuse the predictability of certain highly genetically determined physical traits with the
10 predictability of their personality, cognitive capacity, and character.

11 In addition to concerns about specific harms to children, people have frequently
12 expressed fears that a widespread practice of somatic cell nuclear transfer cloning would
13 undermine important social values by opening the door to a form of eugenics or by tempting
14 some to manipulate others as if they were objects instead of persons. Arrayed against these
15 concerns are other important social values, such as protecting the widest possible sphere of
16 personal choice, particularly in matters pertaining to procreation and child rearing, maintaining
17 privacy, and the freedom of scientific inquiry, and encouraging the possible development of new
18 biomedical breakthroughs.

19 To arrive at its recommendations concerning the use of somatic cell nuclear transfer
20 techniques to create children, NBAC also examined long-standing religious traditions that guide
21 many citizens' responses to new technologies and found that religious positions on human
22 cloning are pluralistic in their premises, modes of argument, and conclusions about human
23 cloning. Some religious thinkers argue that the use of somatic cell nuclear transfer cloning to
24 create a child would be intrinsically immoral and thus could never be morally justified. Other
25 religious thinkers contend that human cloning to create a child could be morally justified under
26 some circumstances, but hold that it should be strictly regulated in order to prevent abuses.

27 The public policies recommended with respect to the creation of a child using somatic
28 cell nuclear transfer reflect the Commission's best judgments about both the ethics of attempting
29 such an experiment and our view of traditions regarding limitations on individual actions in the
30 name of the common good. At present, the use of this technique to create a child would be a
31 premature experiment that would expose the fetus and the developing child to unacceptable risks
32 This in itself is sufficient to justify a prohibition on cloning human beings at this time, even if
33 such efforts were to be characterized as the exercise of a fundamental right to attempt to
34 procreate.

35 Beyond the issue of the safety of the procedure, however, NBAC found that concerns
36 relating to the potential psychological harms to children and effects on the moral, religious, and
37 cultural values of society merited further reflection and deliberation. Whether upon such further
38 deliberation our nation will conclude that the use of cloning techniques to create children would

be allowed or should be permanently banned is an open question. Time is an ally in this regard, allowing for the accrual of further data from animal experimentation, enabling an assessment of the prospective safety and efficacy of the procedure in humans, as well as granting a period of fuller national debate of ethical and social concerns. The Commission therefore concluded that there should be imposed a period of time in which no attempt is made to create a child using somatic cell nuclear transfer. *

Within this overall framework the Commission came to the following conclusions and recommendations.

I. The Commission concludes that at this time it is morally unacceptable for anyone in the public or private sector, whether in a research or clinical setting, to attempt to create a child using somatic cell nuclear transfer cloning. We have reached a consensus on this point because of insufficient information on the safety and effectiveness of this method in humans. Indeed, we believe it would violate important ethical obligations were clinicians or researchers to attempt to create a child using these particular technologies, which are likely to involve substantial risk to the fetus and/or potential child. Moreover, in addition to safety concerns, many other serious ethical concerns have been identified, which require much more widespread and careful public deliberation before this technology may be used.

The Commission, therefore, recommends the following for immediate action:

- A continuation of the current moratorium on the use of federal funding in support of any attempt to create a child by somatic cell nuclear transfer. ✓
- An immediate request to all firms, clinicians, investigators, and professional societies in the private and non-federally funded sectors to comply voluntarily with the intent of the federal moratorium. Professional and scientific societies should make clear that any attempt to create a child by somatic cell nuclear transfer and implantation into a woman's body would at this time be an irresponsible, unethical, and unprofessional act. ✓

II. The Commission further recommends that:

- Federal legislation should be enacted to prohibit anyone from attempting, whether in a research or clinical setting, to create a child through somatic cell nuclear transfer cloning. It is critical, however, that such legislation include a sunset clause to ensure that Congress will review the issue after a specified time period (three to five years) in order to decide whether the prohibition continues to be needed. If state legislation is enacted, it should also contain such a sunset provision. Any such legislation or associated regulation also ought to require that at some point prior to the expiration of the sunset period, an appropriate oversight body will evaluate and report on the current status of somatic cell nuclear transfer technology and on the ethical and social issues that its potential use to ✓

*the use of any other technique ... would raise many of the other non-safety concerns.

create human beings would raise in light of public understandings at that time.

III. The Commission also concludes that:

- Any regulatory or legislative actions undertaken to effect the foregoing prohibition on creating a child by somatic cell nuclear transfer should be carefully written so as not to interfere with other important areas of scientific research. In particular, no new regulations are required regarding the cloning of human DNA sequences and cell lines, since neither activity raises the scientific and ethical issues that arise from the attempt to create children through somatic cell nuclear transfer, and these fields of research have already provided important scientific and biomedical advances. Likewise, research on cloning animals by somatic cell nuclear transfer does not raise the issues implicated in attempting to use this technique for human cloning, and its continuation should only be subject to existing regulations regarding the humane use of animals and review by institution-based animal protection committees.
- If a legislative ban is not enacted, or if a legislative ban is ever lifted, any effort to use the somatic cell nuclear transfer technique to create a child should be preceded by controlled research that is governed by the twin protections of independent review and by existing standards regarding protection of human subjects, including informed consent.
- The United States Government should cooperate with other nations and international organizations to enforce any common aspects of their respective policies on the cloning of human beings.

IV. The Commission also concludes that different ethical and religious perspectives and traditions are divided on many of the important moral issues that surround any attempt to create a child using somatic cell nuclear transfer techniques. Therefore, we recommend that:

- The federal government, and all interested and concerned parties, encourage widespread and continuing deliberation on these issues in order to further our understanding of the ethical and social implications of this technology and to enable society to produce appropriate long-term policies regarding this technology should the time come when present concerns about safety have been addressed. ✓

V. Finally, because scientific knowledge is essential for all citizens to participate in a full and informed fashion in the governance of our complex society, the Commission recommends that:

- Federal departments and agencies concerned with science should cooperate in seeking out and supporting opportunities to provide information and education to the public in the area of genetics, and on other developments in the biomedical sciences where these affect ✓

FINAL DRAFT--JUNE 6, 1997

important cultural practices and commitments.

Chapter One

INTRODUCTION

The idea that humans might someday be cloned—created from a single somatic cell without sexual reproduction—moved further away from science fiction and closer to a genuine scientific possibility on February 23, 1997. On that date, *The Observer* broke the news that Ian Wilmut, a Scottish scientist, and his colleagues at the Roslin Institute were about to announce the successful cloning of a sheep by a new technique. The technique involved transplanting the genetic material of an adult sheep, apparently obtained from a fully differentiated somatic¹ cell, into an egg from which the nucleus had been removed. The resulting birth of the sheep, named Dolly, on July 5, 1996 appears to mark yet another milestone in our ability to control, refine, and amplify the forces of nature.

The Scottish sheep experiment was different from prior attempts to create identical offspring from a pair of adult animals. It used a cloning technique, referred to in this report as "~~somatic cell nuclear transfer~~," to produce an animal that was a genetic twin of an adult sheep. Put another way, Dolly contained the genetic material of only one parent. This technique of transferring a nucleus from a somatic cell into an egg is an extension of research that had been ongoing for over 40 years. The demonstration that somatic cells could be "reprogrammed," or that the genetic complement of the cell could be reactivated well into the chronological life of the cell, is what sets this experiment apart from prior work.

For some time, scientific evidence has suggested that the genetic material contained in differentiated somatic cells may retain the potential to direct the development of healthy fertile adult animals, but its capacity to do so remained unproved (Di Bernadino, 1997). The Roslin experiment, therefore, was a significant scientific event with potentially profound implications since it brings us closer to the possibility of developing a capacity to create clone human beings in an asexual manner. Although for the past ten years scientists have routinely cloned sheep and cows from embryo cells, this was the first successful experiment using the nucleus of a somatic cell to clone an animal that matured to a fully developed state.

from an adult animal

The issues surrounding the cloning of human beings have long been the subject of periodic concern and debate among philosophers, scientists, ethicists, and others, particularly following the publication of Joshua Lederberg's 1966 article on cloning in the *American Naturalist* (Lederberg, 1966). Nevertheless, the impact of these most recent developments on our national psyche has been quite remarkable. Some commentators have suggested that the furor aroused by the new possibility for cloning is out of proportion to most of the ethical, legal,

¹ A somatic cell is any cell of the body other than those destined to become germ cells, i.e., eggs or sperm.

1 and moral issues it raises, since these same issues have been raised by previous developments
2 and are simply emerging again in a novel and striking form. Nevertheless it is important to
3 acknowledge that the possibilities raised by this new technique certainly would be unprecedented
4 and that some would consider its use to be a truly radical step. This type of cloning would
5 involve three novel developments: the replacement of sexual procreation with asexual replication
6 of an existing set of genes; the ability to predetermine the genes of a child; and the ability to
7 create many genetically identical offspring.

8 Some scientists were surprised that the technical barriers of cell differentiation and
9 development seemingly could be so easily overcome when using somatic cells as the source for
10 nuclear transfer. The public—including many members of the scientific community—responded
11 to Dolly with a combination of fascination, hope for useful new understandings of human
12 biology, and profound concern—even alarm—about the prospect of being able to create whole
13 humans from a single somatic cell via nuclear transfer cloning techniques. Although much of the
14 initial public reaction was one of fear, concern, and serious moral reservations about the potential
15 use or abuse of this new technological capacity, a few voices were heard cautiously suggesting
16 that a better understanding of cell dynamics in humans and animals might enable us to develop
17 new cures for various diseases. Thus, it is important to reflect not only on the dangers and
18 ethical reservations but also on the potential human benefits from the use of this type of cloning
19 that might arise in such areas as treating particular infertility problems, transplanting cells or
20 tissues, or preventing certain genetically transmitted harms to offspring.

21 A few of the initial objections to this new type of cloning were either speculative or based
22 on simple misunderstandings, for example, that cloning would allow for the instantaneous
23 creation of a fully grown adult from the cells of an individual. Other fears stemmed from the
24 incorrect idea that an exact copy, although much younger, of an existing person could be made.
25 This fear reflects an erroneous belief that one's genes bear a simple relationship to the physical
26 and psychological traits that make up a person. Although genes provide the building blocks for
27 each individual, it is the interaction among a person's genetic inheritance, the physical and
28 cultural environment, and the process of learning that result in the uniqueness of each individual
29 human. Thus the idea that nuclear transplantation cloning could be used to re-create exemplary or
30 evil people has no scientific basis and is simply false.

31 Other objections to nuclear transplantation cloning, however, are based on carefully
32 articulated philosophical ideals, deep cultural commitments, or religious beliefs, and these
33 deserve continuing and careful consideration. These objections reflect deeply held beliefs about
34 the value of human individuality and personal autonomy, the meaning of family and the value of
35 a child, respect for human life and the natural world, and the preservation of the integrity of the
36 human species.

37 Many public leaders in the United States responded to the announcement about Dolly
38 with immediate and strong condemnation of any attempt to clone human beings in this new

1 manner. The reasons ranged from frightening science fiction imagery to the judgment that
2 cloning of human beings is a serious violation of basic human rights and human dignity. The
3 reaction abroad was similar, with many nations seemingly ready—indirectly or directly—to
4 prohibit cloning human beings in this fashion. Indeed, many international organizations such as
5 UNESCO and the Council of Europe have a long-established and well-articulated concern that
6 research and clinical applications in biology and genetics remain consistent with a fundamental
7 commitment to human dignity and human rights. To date, at least Argentina, Australia, Great
8 Britain, Denmark, Germany, and Spain have enacted laws banning cloning human beings.
9 Unfortunately, some of the deep concerns supporting such views and associated legislation are
10 stated in vague or overly broad terms. The widespread public discomfort, even revulsion, about
11 cloning human beings deserves the best articulation possible, a task that takes time and requires
12 the considered reflections of diverse groups within American society and abroad.

13 Within days of the published report of the apparently successful cloning of a sheep in this
14 new manner, President Clinton instituted a ban on federal funding for research related to cloning
15 of human beings. In addition, the President asked the recently appointed National Bioethics
16 Advisory Commission (NBAC) to address within ninety days the ethical and legal issues that
17 surround the subject of cloning human beings. This provided a welcome opportunity for
18 initiating a thoughtful analysis of the many dimensions of the issue, including a careful
19 consideration of the potential risks and benefits. It also presented an occasion to review the
20 current legal status of cloning and the potential constitutional challenges that might be raised if
21 new legislation were enacted to restrict the creation of a child through somatic cell nuclear
22 transfer.

23 The Commission began its discussions fully recognizing that any effort in humans to
24 transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo, with
25 the apparent potential to be implanted *in utero* and developed to term. Ethical concerns
26 surrounding issues of embryo research have recently received extensive analysis and deliberation
27 in our country. Indeed, federal funding for human embryo research is severely restricted,
28 although there are few restrictions on human embryo research carried out in the private sector.
29 Thus, under current law, the use of somatic cell nuclear transfer to create an embryo solely for
30 research purposes is already restricted in cases involving federal funds. There are, however, no
31 current regulations on the use of private funds for this purpose. NBAC did not review these
32 particular issues in the context of this report. Instead, it focused its attention on the use of such
33 techniques for the purpose of creating an embryo which would then be implanted in a woman's
34 uterus and brought to term. It also expanded its analysis to encompass activities in both the
35 public and private sector.

3

36 Controlling Nature

37 Humankind's efforts to control nature date back as far as recorded history. In particular,
38 domesticated plants and animals have been the mainstay of our agricultural heritage. Over time

human mastery over nature often has been met, quite understandably, with opposition and concern, and frequently has been considered by some to be an affront to the natural order of things or by others to be at odds with interpretations of God's revealed word. Indeed many myths and legends, ancient as well as modern, deal directly with humankind's on-going struggle to ensure that the benefits of our new technological capacities clearly outweigh the harms—both expected and unexpected. The idea that our growing technological mastery is filled with moral ambiguity and capable of both vast good and catastrophic evil is deeply embedded in many cultural traditions.

A prime example is the mythology of the Argo, the first ship, in classical Greek culture. The Greeks see the initial act of shipbuilding as both the origin of culture and the origin of decline. While sailing enables one to encounter other persons and other possibilities, it also brings marauders and war, and its very existence bespeaks the danger of unlimited human desire. Thus, the ability to build and sail boats is both a boon and a curse. Euripides' *Medea* starts with a lament about the trees that were cut down to build the Argo and the other troubles that followed.

Would that the Argo had never winged its way to the land of Colchis....
Would that pine trees had never been felled in the glens of Mount Pelion and
furnished oars for the hands of the heroes who at Pelias' command set forth in
quest of the Golden Fleece.

Concern about our tools and technology has been greatly accelerated with the coming of modern industrialized societies. Is it possible, some now wonder, that our confidence in human competence and technology may be just another myth? How, some are now asking, can we find some moral compass or moral limit to our desire to master everything and possess all? Only such limits, many would say, can save us from the moral ambiguity of our own cleverness.

In recent years, concern about humankind's control over nature has been particularly acute in relation to the new moral choices created by the stunning developments in the biomedical sciences, especially in the area of human reproduction. Although personal reproductive health is considered to be, in most cases, a private matter, ongoing controversies regarding the moral standing of human genetic material and particular human interventions in procreation have focused public attention on the ethical and legal implications of new reproductive techniques. In many cases, initial fears give way to cautious acceptance, but a wariness lingers that is easily reawakened with each new advance.

Artificial insemination by donor, for example, was considered a form of adultery when first introduced in the 1940s. It is now a widely used and accepted practice in the treatment of infertility, although some continue to have serious reservations. When prenatal diagnosis was introduced in the late 1960s, the public simultaneously welcomed the opportunity to prevent lethal disease in newborns but worried about the use of such techniques to select "vanity" characteristics or nonmedical traits in offspring. The birth of Louise Brown, conceived via *in*

1 *vitro* fertilization, in 1978 was another dramatic event, providing a new and controversial means
2 to parenthood. With all of these technical advances, there has been a continuing debate about
3 safety, legality, ethical acceptability, and the government's right to intervene in private matters.

4 Research itself, not just its clinical application, has often sparked debate. For example,
5 research involving human fetuses has been a subject of intense national debate and disagreement
6 for over two decades (Institute of Medicine, 1994). Federal research in this area continues to be
7 restricted to that which has potential therapeutic benefit to the fetus, or involves no more than
8 minimum risk to the fetus even if potential benefit to the mother can be demonstrated.
9 Restrictions also remain regarding embryo research. Despite the recommendations of the
10 National Institutes of Health Human Embryo Research Panel (1994), that certain targeted and
11 carefully regulated research using early human embryos be eligible for federal funds, in
12 December 1994 the President directed NIH not to allocate federal funds for research programs
13 that involved the creation of human embryos solely for research purposes. This issue was also
14 addressed by Congress, which inserted language in the FY96 and FY97 appropriations bills that
15 widened the presidential ban to prohibit virtually all human embryo research conducted with
16 federal funds. Work in this area continues in the United States, but it is largely limited to the
17 private sector, and thus takes place without any federal regulation.

18 Recombinant DNA research represents another example of controversy and intense
19 debate. In the 1970s concerns about the safety of unintended release of recombinant organisms
20 led to a voluntary research moratorium in the scientific community and the development of
21 guidelines (Fredrickson, 1991). Similarly, all experiments involving gene therapy (treatment of
22 specific diseases by inserting human genes into human patients) are subject to review and
23 approval by a federal body.

24 As segments of human DNA or human cells became the focus of study and the objects of
25 manipulation, their use as research materials raised increasingly important ethical issues about
26 how these materials are obtained, transformed, and, in some cases, used to develop commercial
27 products (Office of Technology Assessment, 1987). Such research with human genetic material
28 generates questions about respect for persons and the human body, and the value and moral status
29 to be placed on cells and tissues.

30 Genetic and reproductive technologies also cause concern because of the specter of
31 eugenics and of real or imagined social control through manipulation of human genes. Genetic
32 control suggests broken taboos, and, in the words of Henry David Thoreau, implies that "men
33 have become the tools of their tools"(Blank, 1981). While these concerns are often set against
34 and partly attributable to a backdrop of fiction, fantasy, and misunderstanding, they are, more
35 importantly, related to profound concerns regarding the nature of humankind and its relationship

to other aspects of the natural world.² When the bizarre and fantastic scenarios are removed, we are left with a myriad of reactions: sincere expressions of opposition; serious moral concerns; new hope for a better understanding of human biology and the prospect of combating currently untreatable afflictions; calls for more study; and guarded statements about the need for some measure of control (Macklin, 1994; 1997).

Controlling Science

With some notable exceptions, the scientific community has enjoyed for centuries a great deal of autonomy in directing and regulating its research agenda. Since mid century, however, demands for external regulation have increased, in part because much research, particularly in the biological sciences, is publicly funded and therefore requires some additional measure of accountability. More importantly, society has become more sensitive to concerns about the dangers—particularly to human participants—of the research itself and its future consequences. Further, our evolving moral sensibilities together with the spectacular advances in biomedical science have generated new ethical concerns. As Bernard Davis of Harvard Medical School and others have noted, society sometimes seeks to regulate or restrict research when it poses the specters of dangerous or unfamiliar products, powers, or ideas (Davis, 1980).

The regulation of science has thus become part of the landscape, particularly for those who receive federal funds (Office of Technology Assessment, 1986). In addition to environmental, health, occupational, and safety regulations, scientists must also comply with animal welfare and human subjects protections and abide by restrictions and moratoria on specific types of research. Because science is both a public and social enterprise and its application can have profound impact, society recognizes that the freedom of scientific inquiry is not an absolute right and scientists are expected to conduct their research according to widely held ethical principles. There are times when limits on scientific freedom must be imposed, even if such limits are perceived as an impediment by an individual scientist. Moreover, appropriate ethical constraints are a matter for both scientists and the broader public to formulate and implement. At the same time, limits on freedom of inquiry must be justified, and impositions on such freedom should satisfy certain conditions—for example, that the limits are not arbitrary, that they emerge from the thoughtful balancing of costs and benefits, that they are not unnecessarily oppressive, that they do not lightly impinge on long established rights and freedoms, that there is some continuing public discourse with those affected by the ban, and that such limitations be open to reconsideration in the light of new information and new understanding.

² With respect to interesting fiction consider Aldous Huxley's Brave New World (1932), David Rorvik's unsubstantiated claim of successful human cloning in In His Image (1978), and popular films such as The Boys from Brazil (1978) and Jurassic Park (1993) in which cloning leads to dire, doomsday consequences.

Consideration of Ethical and Religious Perspectives

When the President asked NBAC to take up the issue of the cloning of human beings he admonished that "any discovery that touches upon human creation is not simply a matter of scientific inquiry, it is a matter of morality and spirituality as well." Although well aware that the United States Constitution prohibits the establishment of policies that are *solely* motivated by religious beliefs, NBAC shared the President's concern and sought out testimony about the cloning of human beings from leading scholars from a variety of religious traditions. In the same spirit NBAC also commissioned a background paper on the positions a number of religious traditions have taken or are considering on the cloning of human beings.

NBAC felt this was especially important because religious traditions influence and shape the moral views of many U.S. citizens and religious teachings over the centuries have provided an important source of ideas and inspiration. Although in a pluralistic society particular religious views cannot be determinative for public policy decisions that bind everyone, policy makers should understand and show respect for diverse moral ideas regarding the acceptability of cloning of human beings in this new manner.

Although some religious responses to the cloning of human beings through somatic cell nuclear transfer are tied tightly to particular scriptural texts or other faith commitments, often these ideas can be stated forcefully in terms understandable and persuasive to all persons, irrespective of specific religious beliefs. For example, appeal may be made to a view of human nature or of human reason, rather than exclusively to a religious source of knowledge such as scripture or revelation.

NBAC also wanted to determine whether various religious traditions, despite their distinctive sources of authority and argumentation, reach similar conclusions about this type of human cloning. A convergence of views across these traditions, as well as across secular traditions, would be instructive, even if not necessarily determinative, for public policy.

While many Americans look to their religious faiths for moral guidance on issues, other sources of moral knowledge and insight are also important. Many moral considerations that would be widely acknowledged as legitimate do not depend for their force on particular religious commitments or a specific philosophical outlook. For example, the conviction that it is wrong to harm a child is broadly shared among Americans. If you inquire why it is wrong to harm a child, people may give different answers. Some may refer to their religious convictions that a child is a gift from God. Others may say that it is always wrong to harm an innocent person without some compelling reason. To many people, this is a bedrock principle of ethics, even if it has no single, universally acknowledged foundation in a specific religious or philosophical tradition. Rather, it finds its foundation in many different understandings of morality, some religious, some secular. Moral ideas such as the obligation not to inflict harm on others are accessible to all Americans

and, therefore, can provide a robust foundation for public policy.

America has a vibrant tradition of ethical dialogue in which all are invited to participate. What moral considerations deserve our attention and which are the most important in responding to a particular issue? These are questions that arise with every new controversy. Whether one's ethical beliefs come from theological commitments, philosophical arguments, or from hard-won life experience, all voices should be welcome to the conversation, and all thoughtful views are entitled to a respectful hearing. While tolerance is a widely accepted virtue in American it is important to remind ourselves that it is built on the idea of mutual respect and the capacity to accept, whenever possible, the moral worth of others with whom one may disagree. Tolerance, therefore, means both agreeing to disagree and accepting the challenge of sustaining a community where moral authority will, to some extent, always be contested.

Policy makers, therefore, need to consider a range of moral views when they try to determine whether a particular policy is ethically justifiable as well as politically feasible. A particular policy may not be politically feasible, for instance, if it evokes thoughtful, widespread and vigorous moral opposition. In such circumstances its social costs may outweigh its putative benefits, and additional education and deliberation may be required before new policies are put in place.

Consideration of Law and Public Policy

The public policy chosen with respect to the cloning of human beings via somatic cell nuclear transfer should reflect a keen knowledge of the science, our best judgments about the ethics of attempting such an experiment, and our traditions regarding limitations on individual actions in the name of the common good. Americans in this era, relative to earlier generations, have a wide interest in and substantial knowledge of science. Nevertheless, in the weeks following the report of Dolly the public, the media, and even some scientists demonstrated a surprising lack of understanding of the science involved in cloning. NBAC believes that public debate about issues such as human cloning requires an even more educated populace. Science policy has become public policy, which can be decided wisely only by an informed nation.

American tradition has been to avoid prohibiting or regulating personal activities, absent a compelling reason related to effects on others or society as a whole. Where the individual actions are expressions of fundamental rights, such as the right to free speech or the right to privacy, the reasons for limitation must be compelling, and the limitations made as minimal as possible.

The possibility of cloning human beings in this new fashion appears to raise concerns about direct physical harms to the children who may result. This in itself is sufficient to justify a prohibition on such attempts at this time, even if such efforts were to be characterized as the exercise of a fundamental right to procreate. More speculative psychological harms to the child,

1 and effects on the moral, religious, and cultural values of society may be enough to justify
2 prohibitions in the future, but more time is needed for discussion of these concerns.

3 In its discussion of potential policy options, NBAC considered the relative benefits of
4 achieving an immediate prohibition through federal legislation on cloning human beings using
5 somatic cell nuclear transfer techniques. It also considered more indirect means to deter such
6 experiments.

7 Indirect, non-legislative options considered by NBAC include cooperation by the private
8 sector, both research and clinical, in a moratorium on such experiments and/or clinical practice,
9 and the continued prohibition of the use of federal funds to support such experiments. The
10 American Medical Association, the World Medical Association, and the World Health
11 Organization, for example, have already called for such a moratorium on clinical activities.

12 NBAC also weighed, in terms of nuclear transplantation cloning, the potential impact of a
13 possible legislative measure to extend basic human subjects protections to all research conducted
14 in the United States. This would insure that any research efforts to clone a human in this manner
15 would, along with all other research using human subjects, be covered by the twin protections of
16 informed consent and appropriate scientific review to insure an ethically acceptable balance
17 between risks and benefits. In light of the early state of animal research in this area, such
18 protections should prevent such cloning research from going forward at this time.

19 Finally, NBAC recognized that cooperation with ~~our foreign counterparts~~ ^{other national governments} in the
20 enforcement of any common elements of our respective policies could strengthen any of the
21 measures adopted by the United States. Because science is a global endeavor, cooperation with
22 our foreign counterparts would ensure consistency across borders and enhance public confidence
23 in scientific research generally.

24 Process of NBAC and Organization of the Report

25 The results of NBAC's 90-day analysis are presented in this report. In its deliberations,
26 NBAC focused its discussion on the science of the cloning of human beings using the somatic
27 cell nuclear transfer technique, and the ethical, religious, legal, and regulatory implications of
28 cloning human beings in this manner. To aid in these tasks NBAC invited testimony from an
29 array of scientists, scientific societies, ethicists, theologians, and legal experts, and heard from a
30 wide variety of interested parties during the public comment session at each meeting. In
31 addition, it commissioned numerous background papers from recognized experts to inform its
32 work.

33 This report consists of five chapters in addition to this one. Chapter Two describes the
34 scientific developments that preceded and made possible the cloning of Dolly and speculates on
35 potential applications of this and related technologies. Chapter Three presents some of the key

1 themes in religious interpretations and evaluations of human cloning. Chapter Four outlines the
2 numerous ethical concerns raised by the prospect of cloning human beings via somatic cell
3 nuclear transfer. Chapter Five discusses the legal and policy issues considered by the NBAC as it
4 pondered various recommendations. The final section, Chapter Six, presents the
5 recommendations made by NBAC in response to the President's request.

6 In many instances, NBAC found itself moving at a rapid pace in only partly charted
7 waters. In those times it relied on its individual and collective wisdom, judgment, and moral
8 foundations, and the advice of others. NBAC argued and debated the issues as it searched for
9 appropriate formulations of the problem and for the wisdom to suggest useful policy options.
10 While the members of NBAC learned a great deal during its deliberations, we could not reach a
11 resolution on all of the issues before us. Nevertheless, it was able to accomplish two things.
12 First, it developed a set of recommendations, which are set out in Chapter Six. Second, it agreed
13 that it was important to take a number of steps to ensure the continuation of an informed
14 national discussion of these issues and other developments in the biomedical sciences and
15 clinical practices that have an impact on our moral lives and cultural traditions.

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Chapter Two

THE SCIENCE AND APPLICATION OF CLONING¹

The report in February 1997 that scientists in Scotland had cloned a sheep, Dolly, led to much public discussion of "cloning" of animals and speculation about the possibility of cloning humans. The term "cloning" is used by scientists to describe many different processes that involve making duplicates of biological material. In most cases isolated genes or cells are duplicated for scientific study, and no new animal results. This type of cloning, using genes and cells, has led to many medical advances such as providing insulin to treat diabetes and therapies for hemophilia. The sheep experiment was different: it used a cloning technique called "somatic cell nuclear transfer" and resulted in an animal that was a genetic twin—although delayed in time—of an adult sheep. This technique of transferring a nucleus from a somatic cell into an egg that produced Dolly was an extension of experiments that had been ongoing for over 40 years. These experiments were aimed at understanding how development of an animal from a single fertilized egg is carried out. In recent years the agricultural industry has been trying to improve nuclear transplantation cloning to facilitate the breeding of desirable livestock and some biotechnology companies are exploring ways to use nuclear transfer cloning to improve the production of therapeutic drugs. In addition to drug production, understanding the details of nuclear transplantation cloning might lead to new therapies to treat human disease. For instance it might be possible to grow human cells and tissues for transplantation and grafts that would not be rejected after transfer, as they often are today. These kinds of benefits are currently only hypothetical and much additional research will be needed in animal systems. Although the birth of Dolly was lauded as an amazing success, in fact the procedure is not perfected. Only one sheep was produced from over two hundred nuclear transfers. In addition, it is not yet clear whether Dolly is normal or whether she could have subtle problems that might lead to serious diseases. Using this technique to produce a human child might result in, for example, malformations or disease due to problems inherent in the technique. Thus, while using animals to understand the biological process that produced Dolly holds great promise for future medical advances, there is no current scientific justification for attempting to produce a human child at this time with this technique.

What is Cloning?

The word clone is used in many different contexts in biological research but in its most simple and strict sense, it refers to a precise genetic copy of a molecule, cell, plant, animal, or human

¹ Much of this chapter is derived from the material contained in two commissioned papers provided by Janet Rossant, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto; and by Stuart Orkin, Children's Hospital and Dana Farber Cancer Institute, Boston.

being. In some of these contexts, cloning refers to established technologies that have been part of agricultural practice for a very long time and currently form an important part of the foundations of modern biological research.

Indeed, genetically identical copies of whole organisms are commonplace in the plant breeding world and are commonly referred to as "varieties" rather than clones. Many valuable horticultural or agricultural strains are maintained solely by vegetative propagation from an original plant, reflecting the ease with which it is possible to regenerate a complete plant from a small cutting. The developmental process in animals does not usually permit cloning as easily as in plants. Many simpler invertebrate species, however, such as certain kinds of worms, are capable of regenerating a whole organism from a small piece, even though this is not necessarily their usual mode of reproduction. Vertebrates have lost this ability entirely, although regeneration of certain limbs, organs, or tissues can occur to varying degrees in some animals.

Although a single adult vertebrate cannot generate another whole organism, cloning of vertebrates does occur in nature, in a limited way, through multiple births, primarily with the formation of identical twins. However, twins occur by chance in humans and other mammals with the separation of a single embryo into halves at an early stage of development. The resulting offspring are genetically identical, having been derived from one zygote, which resulted from the fertilization of one egg by one sperm.

At the molecular and cellular level, scientists have been cloning human and animal cells and genes for several decades. The scientific justification for such cloning is that it provides greater quantities of identical cells or genes for study; each cell or molecule is identical to the others.

At the simplest level, molecular biologists routinely make clones of deoxyribonucleic acid (DNA), the molecular basis of genes. DNA fragments containing genes are copied and amplified in a host cell, usually a bacterium. The availability of large quantities of identical DNA makes possible many scientific experiments. This process, often called *molecular cloning*, is the mainstay of recombinant DNA technology and has led to the production of such important medicines as insulin to treat diabetes, tissue plasminogen activator (tPA) to dissolve clots after a heart attack, and erythropoietin (EPO) to treat anemia associated with dialysis for kidney disease.

Another type of cloning is conducted at the cellular level. In *cellular cloning* copies are made of cells derived from the soma, or body, by growing these cells in culture in a laboratory. The genetic makeup of the resulting cloned cells, called a cell line, is identical to that of the original cell. This too, is a highly reliable procedure, which is also used to test and sometimes to produce new medicines such as those listed above. Since molecular and cellular cloning of this sort does not involve germ cells (eggs or sperm), the cloned cells are not capable of developing into a baby.

1 The third type of cloning aims to reproduce genetically identical animals. Cloning of
2 animals can typically be divided into two distinct processes, *blastomere separation* and *nuclear*
3 *transplantation cloning*.

4 In blastomere separation, the developing embryo is split very soon after fertilization when
5 it is composed of two to eight cells (see figure 1). Each cell, called a blastomere, is able to
6 produce a new individual organism. These blastomeres are considered to be totipotent, that is
7 they possess the total potential to make an entire new organism. This totipotency allows
8 scientists to split animal embryos into several cells to produce multiple organisms that are
9 genetically identical. This capability has tremendous relevance to breeding cattle and other
10 livestock.

11 In the early 1980s, a more sophisticated form of cloning animals was developed, known
12 as nuclear transplantation cloning (see figures 2 and 3). The nucleus of somatic cells is
13 diploid—that is, it contains two sets of genes, one from the mother and one from the father.
14 Germ cells, however, contain a haploid nucleus, with only the maternal or paternal genes. In
15 nuclear transplantation cloning, the nucleus is removed from an egg and replaced with the diploid
16 nucleus of a somatic cell. In such nuclear transplantation cloning there is a single genetic
17 "parent," unlike sexual reproduction where a new organism is formed when the genetic material
18 of the egg and sperm fuse (see figure 4). The first experiments of this type were successful only
19 when the donor cell was derived from an early embryo. In theory, large numbers of genetically
20 identical animals could be produced through such nuclear transplantation cloning. In practice,
21 the nuclei from embryos which have developed beyond a certain number of cells seem to lose
22 their totipotency, limiting the number of animals that can be produced in a given period of time
23 from a single, originating embryo.

24 The new development in the experiments that Wilmut and colleagues carried out to
25 produce Dolly was the use of much more developed somatic cells isolated from adult sheep as
26 the source of the donor nuclei. This achievement of gestation and live birth of a sheep using an
27 adult cell donor nucleus was stunning evidence that cell differentiation and specialization are
28 reversible. Given the fact that cells develop and divide after fertilization and differentiate into
29 specific tissue (e.g., muscle, bone, neurons), the development of a viable adult sheep from a
30 differentiated adult cell nucleus provided surprising evidence that the pattern of gene expression
31 can be reprogrammed. Until this experiment many biologists believed that reactivation of the
32 genetic material of mammalian somatic cells would not be complete enough to allow for the
33 production of a viable adult mammal from nuclear transfer cloning.

34 The Science That Led to Dolly

35 Until the birth of Dolly, developmental and molecular biologists focused their efforts on
36 understanding the processes of cellular differentiation, the regulation of genes during this
37 process, the factors that stimulate differentiation, and the reversibility of this process. Biologists

have investigated whether, once cellular differentiation occurs, the process is reversible. These questions have by no means been fully answered by the appearance of Dolly. If anything, the existence of Dolly stimulates even more speculation and inquiry. This section describes the background of the science that led to the birth of the cloned sheep, including early studies of differentiation and development, research on regulation of gene expression, experiments using nuclear transfer in animals, and studies of cell programming and division.

Early Studies of Differentiation and Development

Nearly every cell contains a spheroid organelle called the nucleus which houses nearly all the genes of the organism. Genes are composed of DNA, which serve as a set of instructions to the cell to produce particular proteins. Although all somatic cells contain the same genes in the nucleus, the particular genes that are activated vary by the type of cell. For example, a differentiated somatic cell, such as a neuron, must keep a set of neural-specific genes active and silence those genes specific to the development and functioning of other types of cells such as muscle or liver cells.

Investigations which began over 40 years ago sought to determine whether a differentiated somatic cell still contained all genes, even those it did not express. Early experiments in frogs and toads by Gurdon (1962) and by Briggs and King (1952) provided strong evidence that the expression potential of the genes in differentiated cells is essentially unchanged from that of the early embryo. Nuclei from donor differentiated cells were injected into recipient eggs in which the nucleus had been inactivated (figure 2). The first series of experiments used cells from tadpoles as the source of donor nuclei (Gurdon, 1962) and adult frogs were produced, albeit at a very low efficiency. Although the cells used were highly specialized, they were not derived from the adult frog, so the cells might not have been fully differentiated.

In these experiments, because isolated nuclei were used, other cellular components were not transferred to the recipient egg. Among those other cellular components is an organelle called the mitochondrion, the energy-producing component of the cell. Although most of the genes specifying this cellular component reside in the nucleus, the mitochondrion itself houses some genes. Thus, in somatic cell nuclear transfer, mitochondrial genes are not transferred to the enucleated egg along with the nuclear genes. Because there are some serious diseases carried by mitochondria, nuclear transplantation could allow a cell to develop with new, healthy mitochondria from a donor.

Gurdon and colleagues performed another carefully controlled series of experiments in which they used nuclei from adult frog skin cells for transfer to an enucleated egg (Gurdon, et al., 1975). Four percent of the nuclei transferred eventually gave rise to fully developed tadpoles. These experiments provided evidence that the genes contained in the nuclei of differentiated cells could be reactivated by the cytoplasm of the egg and thus direct normal development, but only up to a certain stage. No viable adult frog ever developed from these tadpoles and there was a

decrease in the number of tadpoles born as the age of the transferred nucleus increased. This left open the possibility that complete reactivation of the adult nucleus was prevented by some irreversible change in the genetic material, and that there was a progressive decline in nuclear potential with age.

Careful analysis, however, suggested that the major reason for developmental failure of the transplanted embryos appeared to be chromosomal abnormalities that occurred during the process of nuclear transplantation itself. The rate of cell division of adult cells is much slower than that of the cells of the early frog embryo. Thus, in reality, for this technique to work it would be necessary that the transplanted adult nucleus reprogram its gene expression, replicate its DNA, and enter the normal embryonic cell division cycle within an hour of nuclear transfer. It is remarkable, given the mechanics and timing of the process, that any nuclei from adult somatic cells were successful in generating an embryo. Although they did not produce normal adult animals, the amphibian nuclear transfer experiments of Gurdon and others succeeded in demonstrating that the differentiated state of adult somatic cells do not involve major irreversible changes in their DNA.

Regulation of Gene Expression

In recent years, it has been determined that most patterns of differentiated gene expression are maintained by active control mechanisms, in which particular genes are turned on or off by regulatory proteins (Blau, 1992). Further studies suggested that it might be possible to reprogram the gene expression of somatic cells so that they perform a different task. The role of a particular cell type (e.g., muscle, liver, or skin) depends on the combination of regulatory proteins it expresses. While in certain specialized cells, such as white blood cells, actual rearrangements and deletions of DNA occur, for the most part, however, gene expression is not regulated by the loss of DNA but by the turning off of specific genes. Thus, it should be possible to activate or inactivate almost any gene in a cell, given the right cellular environment containing the appropriate regulatory molecules.

To reprogram the gene expression of a somatic cell it is not essential to fuse it with an egg; in some cases re-programming can occur through fusion of two adult cells. Cell fusion experiments, in which different somatic cell types are fused, have demonstrated that extensive reprogramming of differentiated nuclei can occur. For example, when muscle cells are fused with non-muscle cells of various sorts, muscle-specific genes are activated in the non-muscle cells (Blau et al., 1985), and, similarly, genes that code for hemoglobin can be activated in many cell types after fusion with red blood cells (Baron and Maniatis, 1986). These and other kinds of experiments have led to the isolation of specific factors that regulate cell differentiation, such as the gene that regulates the formation of muscle cells (Weintraub, 1993).

These studies have further demonstrated that the stability of the differentiated state is not absolute. Thus, given the appropriate regulatory molecules and enough time to reprogram an

adult nucleus, somatic cells can re-initiate earlier programs of differentiation.

Nuclear Transfer in Mammals

Experiments in mammals have also suggested that it is possible to reprogram adult somatic cells. Following success in the nuclear transfer experiments in frogs, scientists attempted to repeat the experiments in mice. It was known that early development occurs at a considerably slower rate in mammals than amphibians, giving hope that reprogramming of the donor nucleus would occur more efficiently. For example, the first cell division in mice occurs about a day after fertilization, giving ample time, it was thought, for the reprogramming of gene expression and adjustment of the cell division cycle. This proved not to be the case. Early experiments showed that nuclei from somatic cells fused with fertilized eggs did not undergo nuclear division (Graham, 1969).

However, a series of experiments in mice in the mid 1980s showed that nuclei could be successfully exchanged between fertilized eggs, with 90 percent reaching the blastocyst stage of embryonic development and beyond (McGrath and Solter, 1984). Nuclei recovered and transplanted from embryos at the two-cell stage could direct development to the blastocyst stage. Nuclei transferred from embryos at later stages, however, could not successfully recapitulate development. In fact, in mice, nuclei show less totipotency than whole cells. Many experiments have shown that blastomeres up to the early blastocyst stage are still totipotent when combined with other embryonic cells (Rossant and Pedersen, 1986). This means that the failure of nuclear reprogramming has to be the result of something other than irreversible changes to the genetic material of the cells. In 1986, Willadsen reported experiments with sheep. Unlike the situation in mice, enucleated eggs from sheep could be fused with blastomeres taken from embryos at the eight-cell stage to provide donor nuclei and viable offspring were produced (Willadsen, 1986).

Recent experiments have used nuclear transfer into enucleated unfertilized eggs (figure 3). Using these very early stage eggs prolongs the period of possible reprogramming before the donor nucleus has to undergo the first division. And the advent in the last few years of electrofusion for both fusion of cells and activation of the egg has been another major advance, because activation and fusion occur simultaneously. Because these experiments use fusion of two cells and not simple injection of an isolated nucleus, all of the cellular components are transferred. Thus, the mitochondria, which contain some genes of their own, are transferred along with the nucleus. Because an enucleated egg also contains mitochondria, the result of a fusion experiment is a cell with a mixture of mitochondria from both the donor and the recipient. Since the mitochondrial genes represent an extremely small proportion of the total number of mammalian genes, mixing of mitochondria per se is not expected to have any major effects on the cell. However, if one of the donors suffers from a mitochondrial disease, then mixture of the mitochondria may significantly alleviate the disease.

Over the past ten years or so there have been numerous reports of successful nuclear transfer experiments in mammals, nearly all of them using cells taken directly from early embryos. The oldest embryonic nucleus that can successfully support development differs among species. Four-cell blastomere nuclei have been successfully used in pigs (Prather, et al., 1989). In mice, no nucleus older than the eight-cell stage has been used successfully (Cheong, et al., 1993). In rabbits, 32- to 64-cell early embryos can be used as nuclear donors (Yang, et al., 1992). In cows and sheep, cells from what is called the inner cell mass (ICM) of the 120-cell blastocyst stage (see figure 1) have been used successfully (Collas and Barnes, 1994; Smith and Wilmut, 1989). Indeed, in both cows and sheep, cell lines have been made from these ICM cells and nuclei from these cells have been used to reprogram development after transfer into enucleated unfertilized eggs.

In the first experiments of this sort by Sims and First (1994), cow cells derived from embryos were grown in the laboratory for up to 28 days, and then used as nuclear donors, without any attempt at synchronization of the cell division cycle of the donor cells. Of those successfully fused with eggs, 24 percent developed to the blastocyst stage, and 4/34 (12 percent) of the blastocysts transferred to recipient cows developed into normal calves. This success rate compares favorably with those seen using earlier blastomeres and suggests that it might be possible to achieve successful nuclear transfer from permanent cell lines established from early embryos.

Reprogramming of Nuclei and Synchronization of the Cell Division Cycle

There has been some study of the events that occur once a transferred nucleus is exposed to the cytoplasm of the egg and some, but not all, of the parameters that affect success of nuclear transfer are known (Fulka, et al., 1996). Enucleated eggs used for fusion only proceed to division after activation by some artificial signal, such as the electrical current used in the electrofusion technique. When donor nuclei are introduced into the enucleated egg, they usually undergo DNA replication, nuclear envelope breakdown, and chromosome condensation. After activation of the egg the nuclear envelope is reformed around the donor chromosomes. The nucleus now takes on the appearance of a typical egg nucleus at this stage, which is large and swollen. It is assumed that this process begins the reprogramming of the transferred donor nucleus by exposing the chromosomes to the egg cytoplasm and beginning the exchange of egg-derived proteins for the donor nucleus' own proteins (Prather and First, 1990).

It is not clear whether exposure to proteins found in the earliest stages of development and/or nuclear swelling is a prerequisite for reprogramming for later development. Experiments in a number of species have shown that, when nuclei are fused with eggs that have been activated some hours prior to fusion, no DNA replication, chromosome condensation, or nuclear swelling occurs, but normal development can transpire (Campbell, et al., 1994; Stice, et al., 1994).

It is not clear which of the processes described above are required for normal

development. In rabbits, cows, sheep, and mice (Cheong, et al., 1993; Collas, et al., 1992) experiments have shown that nuclei from cells in the early phases of the cell division cycle do better than cells in later stages. In the first phase of the cell cycle, termed G1 (for Gap phase 1), cells contain only one complete set of chromosomes and are relatively quiescent. They then enter a period of DNA synthesis or replication, called S-phase, followed by a rest phase, called G2 (Gap phase 2), at which time they each have a duplicate copy of each chromosome. This doubling of the chromosomes is in preparation for cell division where an equal number will be divided between the two daughter cells. Because DNA replication is induced *after* nuclear transfer, any nucleus that has initiated replication *before* transfer will end up with too much DNA, which will likely result in chromosome anomalies. Thus, the need to transfer nuclei in the G1 phase before replication is initiated, is likely to be important to avoid chromosome damage that will prevent development of the embryo into a viable offspring.

Changes in Technique that Allowed for the Birth of Dolly

In background work that preceded the birth of Dolly, Wilmut and colleagues established cell lines from sheep early embryos, or blastocysts, and used these cells as nuclear donors (Campbell, et al., 1996). In an attempt to avoid the problems of nuclear transfer of non-G1 nuclei into activated eggs, they starved the donor cell line by removing all nutrients from the medium prior to nuclear transfer. Under these starvation conditions, the cells exit the cell cycle and enter the so-called "G0" state (Gap phase 0), similar to the G1 phase in which chromosomes have not replicated. Fusion of G0 nuclei with eggs ensures that the donor chromosomes have not initiated replication prior to fusion. It was also suggested that the G0 state might actually increase the capacity of the nucleus to be reprogrammed by the egg cytoplasm. However, there is currently no direct evidence to support this, nor to conclude that nuclei synchronized in the G0 stage are any better than nuclei synchronized in G1. For Wilmut and colleagues, approximately 14 percent of fusions resulted in development of blastocysts, and 4/34 (12 percent) embryos transferred developed into live lambs. Two died shortly after birth. The success rate in sheep and cow experiments was almost identical, and suggests that division of cells in culture for many days does not inhibit the ability of their nuclei to be reprogrammed by the egg environment. Could the same be true of nuclei from fully differentiated somatic cells?

All of this background work led up to Dolly (Wilmut, et al., 1997). Wilmut and colleagues took late embryo, fetal cell cultures, and cell cultures derived from the mammary gland of an adult sheep and applied the same approach of synchronizing the cells in the G0 stage prior to nuclear transfer. They reported successful production of live offspring from all three cell types, although only 29 of 277 (11 percent) of successful fusions between adult mammary gland nuclei and enucleated oocytes developed to the blastocyst stage, and only 1 of 29 (3 percent) blastocysts transferred developed into a live lamb. This experiment was, in fact, the first time any fully developed animal had been born following transfer of a somatic cell nucleus, since the earlier frog experiments only generated tadpoles.

1 It should be noted, however, that the amount of new information regarding the stability of
2 the differentiated state derived from this experiment is small, as no attempt was made to
3 document that the donor cells were fully differentiated cells, the genes of which expressed
4 specialized mammary gland proteins. In the earlier experiments with frogs, the fact that the
5 donor cells were fully differentiated was documented in such a manner. In the present case, Dolly
6 could have been derived from a less-differentiated cell in the population, such as a mammary
7 stem cell.

8 **Remaining Scientific Uncertainties**

9 Several important questions remain unanswered about the feasibility in mammals of
10 nuclear transfer cloning using adult cells as the source of nuclei:

11 First, can the procedure that produced Dolly be carried out successfully in other cases?
12 Only one animal has been produced to date. Thus, it is not clear that this technique is
13 reproducible even in sheep.

14 Second, are there true species differences in the ability to achieve successful nuclear
15 transfer? It has been shown that nuclear transfer in mice is much less successful than in larger
16 domestic animals. Part of this difference may reflect the intensity of research in this area in the
17 last ten years; agricultural interests have meant that more nuclear transfer work has been
18 performed in domestic animals than in mice. But part of the species differences may be real and
19 not simply reflect the greater recent effort in livestock. For example, in order for a differentiated
20 nucleus to redirect development in the environment of the egg, its constellation of regulatory
21 proteins must be replaced by those of the egg in time for the embryo to use the donor nucleus to
22 direct normal development of the embryo. The species difference may be the result of the
23 different times of embryonic gene activation.

24 In mammals, unlike many other species, the early embryo rapidly activates its genes and
25 cannot survive on the components stored in the egg. The time at which embryonic gene
26 activation occurs varies between species—the late 2-cell stage in mice (Schultz, 1993), the 4-8
27 cell stage in humans (Braude, et al., 1988) and the 8-16 cell stage in sheep. The later onset of
28 embryonic gene activation and transcription in sheep provides an additional round or two of cell
29 divisions during which nuclear reprogramming can occur, unlike the rapid genome activation in
30 the mouse. Further cross-species comparisons are needed to assess the importance of this
31 difference in the time of genome activation for the success of nuclear transfer experiments. In
32 humans, for example, the time period before gene activation is very short, which might not
33 permit the proper reprogramming of genes after nuclear transfer to allow for subsequent normal
34 development.

35 Third, will the phenomenon of genetic imprinting affect the ability of nuclei from later
36 stages to reprogram development? In mammals imprinting refers to the fact that the genes

1 inherited on the chromosomes from the father (paternal genes) and those from the mother
2 (maternal genes) are not equivalent in their effects on the developing embryo (Solter, 1988).
3 Some heritable imprint is established on the chromosomes during the development of the egg and
4 the sperm such that certain genes are expressed only when inherited from the father or mother.
5 Imprinting explains why parthenogenetic embryos, with only maternally inherited genes, and
6 androgenetic embryos, with only paternally inherited genes, fail to complete development
7 (Fundelev and Surani, 1994). Nuclei transferred from diploid cells, whether embryonic or adult,
8 should contain maternal *and* paternal copies of the genome, and thus not have an imbalance
9 between the maternally and paternally derived genes.

10 The successful generation of an adult sheep from a somatic cell nucleus suggests that the
11 imprint can be stable, but it is possible that some instability of the imprint, particularly in cells in
12 culture, could limit the efficiency of nuclear transfer from somatic cells. It is known that
13 disturbances in imprinting lead to growth abnormalities in mice and are associated with cancer
14 and rare genetic conditions in children.

15 Fourth, will cellular aging affect the ability of somatic cell nuclei to program normal
16 development? As somatic cells divide they progressively age and there is normally a defined
17 number of cell divisions that they can undergo before senescence. Part of this aging process
18 involves the progressive shortening of the ends of the chromosomes, the telomeres, and other
19 genetic changes. Germ cells (eggs and sperm) evade telomere shortening by expressing an
20 enzyme, telomerase, that can keep telomeres full length. It seems likely that returning an adult
21 mammalian nucleus to the egg environment will expose it to sufficient telomerase activity to
22 reset telomere length, since oocytes have been found to be potent sources of telomerase activity
23 (Mantell and Greider, 1994).

24 Fifth, will the mutations that accumulate in somatic cells affect nuclear transfer efficiency
25 and lead to cancer and other diseases in the offspring? As cells divide and organisms age,
26 mistakes and alterations (mutations) in the DNA will inevitably occur and will accumulate with
27 time. If these mistakes occur in the sperm or the egg, the mutation will be inherited in the
28 offspring. Normally mutations that occur in somatic cells affect only that cell and its descendants
29 which are ultimately dispensable. Nevertheless, such mutations are not necessarily harmless.
30 Sporadic somatic mutations in a variety of genes can predispose a cell to become cancerous.
31 Transfer of a nucleus from a somatic cell carrying such a mutation into an egg would transform a
32 sporadic somatic mutation into a germline mutation that is transmitted to all of the cells of the
33 body. If this mutation were present in all cells may lead to a genetic disease or cancer. The risks
34 of such events occurring following nuclear transfer are difficult to estimate.

35 Why Pursue Animal Cloning Research?

36 Research on nuclear transfer cloning in animals may provide information that will be
37 useful in biotechnology, medicine, and basic science. Some of the immediate goals of this

research are:

- to generate groups of genetically identical animals for research purposes
- to rapidly propagate desirable animal stocks
- to improve the efficiency of generating and propagating transgenic livestock
- to produce targeted genetic alterations in domestic animals
- to pursue basic knowledge about cell differentiation

Cloning Animals for Research Purposes

Inbred strains of mice have been a mainstay of biological research for years because they are essentially genetically identical and homozygous (i.e., both copies of each gene inherited from the mother and father are identical). Experimental analysis is simplified because differences in genetic background that often lead to experimental variation are eliminated. Generating such homozygous inbred lines in larger animals is difficult and time consuming because of the long gestation times and small numbers of offspring. The concept of generating small groups of identical animals by nuclear transfer has been proposed as an alternative strategy to obtaining a genetically identical group of animals, and apparently underlies a recent report from Oregon on successful nuclear transfer from early embryonic nuclei in rhesus macaque monkeys (Weiss and Schwartz, 1997).

Repeated cycles of nuclear transfer can expand the number of individual animals derived from one donor nucleus, allowing more identical animals to be generated. The first nuclear transfer embryo is allowed to divide to early blastomere stages and then those cells are used as donor nuclei for another series of transfers. This process can be carried on indefinitely, in theory, although practice suggests that successful fusion rates decline with each cycle of transfer. One experiment in cows, for example, produced 54 early embryos after three cycles of transfer from a single blastomere nucleus from one initial embryo (Stice and Keefer, 1993). Viable calves were produced from all three cycles of nuclear transfer.

This approach is likely to be limited in its usefulness, however. A group of cloned animals derived from nuclear transfer from an individual animal is self-limited. Unless they are derived from an inbred stock initially, each clone derived from one individual will differ genetically from a clone derived from another individual. Once a cloned animal is mated to produce offspring, the offspring will no longer be identical due to the natural processes which shuffle or recombine genes during development of eggs and sperm. Thus each member of a clone has to be made for each experiment by nuclear transfer, and generation of a large enough number of cloned animals to be useful as experimental groups is likely to be prohibitively expensive in most animals.

Advantages of Nuclear Transfer Cloning for Breeding Livestock

In animal breeding, the rapid spread of certain traits within stocks of domestic animals is of obvious commercial importance and has very long historical standing. Artificial insemination and embryo transfer can increase the effective reproductive output of individual elite male and female animals and are widely used in the livestock industry. Nuclear transfer cloning, especially from somatic cell nuclei, could provide an additional means of expanding the number of chosen livestock. The ability to make identical copies of adult prize cows, sheep, and pigs is a feature unique to nuclear transfer technologies, and may well be used in livestock production, if the efficiencies of adult nuclear transfer can be improved. The net effect of multiplying chosen animals by cloning will be to reduce the overall genetic diversity in a given livestock line, likely with severe adverse long-term consequences. If this technique became widespread, efforts would have to be made to ensure a pool of genetically diverse animals for future livestock maintenance.

Improved Generation and Propagation of Transgenic Livestock

There is considerable interest in being able to genetically alter farm animals by introduction and expression of genes from other species, such as humans. So-called "transgenic animals" were first developed using mice, by microinjection of DNA into the nucleus of the egg. This ability to add genes to an organism has been a major research tool for understanding gene regulation and for using the mouse as a model in studies of certain human diseases. It has also been applied to other species including livestock. Proposed applications of this technology to livestock improvement include the possible introduction of growth-enhancing genes, genes that affect milk quality or wool fibers, or disease-resistance genes (Ward and Nancarrow, 1995). But progress has been slow. Initial results of the manipulation of meat production by expression of excess growth hormone in pigs led to undesirable side effects (Pursel, et al., 1989).

Currently, the major activity in livestock transgenesis is focused on pharmaceutical and medical applications. The milk of livestock animals can be modified to contain large amounts of pharmaceutically important proteins such as insulin or factor VIII for treatment of human disease by expressing human genes in the mammary gland (Houdebine, 1994). In sheep greater than 50 percent of the proteins in milk can be the product of a human gene (Colman, 1996). The milk of even transgenic mice can yield large (milligram) quantities of recombinant proteins. Since many such proteins are active at very low concentrations, it is estimated that production of human drugs from transgenic animals could be considerably more cost-effective than current methods.

Another major area of interest is the use of transgenic animals for organ transplantation into humans. Pig organs, in many cases, are similar enough to humans to be potentially useful in organ transplants, if problems of rejection could be overcome. Rejection can already be partly overcome by the expression of human complement (a component of the immune system) regulatory proteins in transgenic pigs. Further transgenic manipulation such as the expression of human antigens in pigs could alleviate organ shortages by minimizing or eliminating the rejection of pig organs transplanted into humans, although other barriers, such as the possible transmission of viruses from pigs to humans, must be overcome.

However the current method of directly injecting genes into fertilized eggs is inefficient. Not all injected eggs will develop into transgenic animals, and then not all transgenic animals will express the added gene in the desired manner. The production of transgenic livestock is slow and expensive. Nuclear transfer would speed up the expansion of a successful transgenic line, but, perhaps more importantly, it would allow more efficient generation of transgenic animals in the first place. Foreign DNA, such as a human gene, could be introduced into cell lines in culture and cells expressing the transgene could be characterized and used as a source of donor nuclei for cloning, and all offspring would likely express the human gene. This, in fact, was the motivation behind the experiments that led to the production of Dolly. If a human gene such as that for insulin could be expressed in the mammary gland, the milk of the sheep would be an excellent source of insulin to treat diabetes.

Generating Targeted Gene Alterations

The most powerful technology for gene replacement in mammals was developed in mice. This technique adds manipulated or foreign DNA to cells in culture to replace the DNA present in the genome of the cells. Thus mutations or other alterations that would be useful in medical research can be introduced into an animal in a directed and controlled manner and their effects studied, a process called *gene targeting* (Capecchi, 1989). This technology would be of limited use, however, without some means of taking the changes generated in cultured cells and reintroducing them into animals. In mice, this can be achieved by the use of embryonic stem (ES) cells that are capable of being cultured indefinitely in the undifferentiated state. ES cells retain the potential to form all cells of the animal, including the germ cells, when returned to the environment of the early embryo (figure 5). As the technique is currently used in mice, the first generation of animals generated from the ES cells are "chimeric," that is, they are made up of a mixture of cells from two different animals. These mice must then be bred one more time to transmit altered genes to the next generation. Using this technique, any genetic alteration made in the embryonic stem cells in culture can be introduced back into mice (Robertson, 1986).

This use of gene replacement and embryonic stem cell technology has been responsible for the explosion in the generation of "knock-out" mice, in which specific genes have been deleted from the genome. These mice have been invaluable in current studies to understand normal gene function and to allow the generation of accurate models of human genetic disease. Gene targeting approaches can also be used to ensure correct tissue-specific expression of foreign genes and to suppress the expression of genes in inappropriate tissues. If applied to domestic animals, this technology could increase the efficiency of the expression of foreign genes by targeting the introduced genes to appropriate regions of the chromosome. It could also be used to directly alter the normal genes of the organism, which could influence animal health and productivity or to help develop transgenic organs that are less likely to be rejected upon transplantation. However, to date, there are no fully validated embryonic stem cell lines in domestic animals. Nuclear transfer from somatic cell lines into an egg, as reported by Wilmut and colleagues, provides a possible alternative to the embryonic stem cell route for introduction

of targeted gene alterations into the germ line of animals.

Apart from the fact that embryonic stem cell lines have not yet been produced from farm animals, the other argument for using nuclear transfer to introduce germ line genetic alterations in farm animals is that it eliminates one generation of breeding from the initial chimeric animals. This is an important time and cost saving factor in farm animals with long generation times and small litter size. However this factor might not be as important as once thought. In mice, it turns out, embryonic stem cells can also be used to generate cloned animals carrying gene alterations directly without the initial generation of chimeric animals. When 'tetraploid' embryos that are not themselves capable of developing normally, are used as the host cells, the entire mouse fetus can be derived directly from the normal diploid ES cells (figure 6)(Nagy, et al., 1993). Although this procedure is not yet very efficient, it illustrates the remarkable properties of ES cells and suggests that similar approaches could be applied in other species such as farm animals.

Basic Research on Cell Differentiation

The basic cellular processes that allowed the birth of Dolly by nuclear transfer using the nucleus from an adult somatic donor cell are not well understood. If indeed the donor cell was a fully differentiated cell and not a rare, less differentiated stem cell that resulted in this cloned sheep, there will be many questions to ask about how this process occurred. How the specialized cell from the mammary gland was reprogrammed to allow the expression of a complete developmental program will be a fascinating area of study. Developmental biologists will want to know which genes are reprogrammed, when they are expressed, and in what order. This might shed light on the still poorly understood process of sequential specialization that must occur during development of all organisms.

Molecular biologists will also likely learn much from studying how reprogramming and reactivation occurred. What regulatory proteins in the host egg participated in the reprogramming? How did these proteins interact with each other and the DNA so that inactive genes from the mammary gland cells might be activated again? Answers to these kinds of questions will contribute to our overall understanding of how cells grow, divide, and become specialized.

Basic research into these fundamental processes may also lead to the development of new therapies to treat human disease. It is not possible to predict from where the essential new discoveries will come. However, already the birth of Dolly has sparked ideas about potential benefits that might be realized. To explore the possibility of these new therapies, extensive basic research is needed.

Much of this basic research will likely be done in the mouse as this animal is widely used by developmental biologists, and thus a great deal is already known about its development. However, as described above, the use of cloning in other animals—such as cows, pigs and

sheep—by agricultural and biotechnology companies will also contribute to understanding of the basic processes involved. The study of nuclear transplantation cloning in a wide variety of animals will be very useful. Although many of the basic cellular mechanisms underlying animal development are the same in all mammals, there are subtle developmental variations that often lead to major technical differences in working with a particular species. Because a technique is often perfected in one species before being applied to another, knowing which parts of the techniques are widely applicable and which might need to be perfected for the given species will be of great value. This body of research into animal systems will answer many questions about the feasibility of various new therapeutic applications being proposed for human cells. New innovations in treating human disease can be tested in animal systems to determine if the basic foundation of the idea is sound before experiments using human cells would be required. Thus the path to testing the potential therapies to treat human disease, described below, should initially go through testing in animal models before progressing to human cell research.

Potential Therapeutic Applications of Nuclear Transfer Cloning

The demonstration that, in mammals as in frogs, the nucleus of a somatic cell can be reprogrammed by the egg environment provides further impetus to studies on how to reactivate embryonic programs of development in adult cells. These studies have exciting prospects for regeneration and repair of diseased or damaged human tissues and organs, and may provide clues as to how to reprogram adult differentiated cells directly without the need for oocyte fusion. In addition, the use of nuclear transfer has potential application in the field of assisted reproduction.

Potential Applications in Organ and Tissue Transplantation

Many human diseases, when they are severe enough, are treated effectively by organ or tissue transplantation, including some leukemias, liver failure, heart and kidney disease. In some instances the organ required is non-vital, that is, it can be taken from the donor without great risk (e.g., bone marrow, blood, kidney). In other cases, the organ is obviously vital and required for the survival of the individual, such as the heart. All transplantation is imperfect, with the exception of that which occurs between identical twins, because transplantation of organs between individuals requires genetic compatibility.

In principle, the application of nuclear transfer cloning to humans could provide a potential source of organs or tissues of a predetermined genetic background. The notion of using human cloning to produce individuals for use solely as organ donors is repugnant, almost unimaginable, and morally unacceptable. A morally more acceptable and potentially feasible approach is to direct differentiation along a specific path to produce specific tissues (e.g., muscle or nerve) for therapeutic transplantation rather than to produce an entire individual. Given current uncertainties about the feasibility of this, however, much research would be needed in animal systems before it would be scientifically sound, and therefore potentially morally acceptable, to go forward with this approach.

Potential Applications in Cell-based Therapies

Another possibility raised by cloning is transplantation of cells or tissues not from an individual donor but from an early embryo or embryonic stem cells; the primitive, undifferentiated cells from the embryo that are still totipotent. This potential application would not require the generation and birth of a cloned individual. Embryonic stem cells provide an interesting model for such studies, since they represent the precursors of all cell lineages in the body. Mouse embryonic stem cells can be stimulated to differentiate *in vitro* into precursors of the blood, neuronal and muscle cell lineages, among others (Weiss and Orkin, 1995), and they thus provide a potential source of stem cells for regeneration of all tissues of the body. ✓

It might be possible to take a cell from an early blastomere and treat it in such a manner as to direct its differentiation along a specific path. By this procedure it might be possible to generate in the laboratory sufficient numbers of specialized cells, for example bone marrow stem cells, liver cells, or pancreatic beta-cells (which produce insulin) for transplantation. If even a single tissue type could be generated from early embryonic cells by these methods and used clinically, it would constitute a major advance in transplantation medicine by providing cells that are genetically identical to the recipient.

One could imagine the prospect of nuclear transfer from a somatic cell to generate an early embryo and from it an embryonic stem cell line for each individual human, which would be ideally tissue-matched for later transplant purposes. This might be a rather expensive and far-fetched scenario. An alternative scenario would involve the generation of a few, widely used and well characterized human embryonic stem cell lines, genetically altered to prevent graft rejection in all possible recipients.

The preceding scenarios depend on using cells of early human embryos, generated either by *in vitro* fertilization or nuclear transfer into an egg. Because of ethical and moral concerns raised by the use of embryos for research purposes it would be far more desirable to explore the direct use of human cells of adult origin to produce specialized cells or tissues for transplantation into patients. It may not be necessary to reprogram terminally differentiated cells but rather to stimulate proliferation and differentiation of the quiescent stem cells which are known to exist in many adult tissues, including even the nervous system (Gage, et al., 1995). Experiments in this area are likely to focus more on the conditions required for direct stimulation of the stem cells in specific tissues, than actual use of nuclear transfer to activate novel developmental programs. These approaches to cellular repair using adult stem cells will be greatly aided by an understanding of how stem cells are established during embryogenesis.

Another strategy for cell-based therapies would be to identify methods by which somatic cells could be "de-differentiated" and then re-differentiated along a particular path. This would eliminate the need to use cells obtained from embryos. Such an approach would permit the

growth of specialized cells compatible with a specific individual person for transplantation. Although at the current time this strategy is highly speculative, ongoing research in animal systems may identify new approaches or new molecular targets that might make this approach feasible.

It will be of great importance to understand through experiments in animals how the environment of the egg reprograms a somatic cell nucleus. What cellular mechanisms can be elucidated? What components are involved in these processes? Can we direct cells along particular developmental pathways in the laboratory and use these cells for therapy? The capacity to grow human cells of different lineages in culture would also dramatically improve prospects for effective somatic gene therapy.

Assisted Reproduction

Another area of medicine where the knowledge gained from animal work has potential application is in the area of assisted reproduction. Assisted reproduction technologies are already widely used and encompass a variety of parental and biological situations, that is, donor and recipient relationships. In most cases, an infertile couple seeks remedy through either artificial insemination or in vitro fertilization using sperm from either the male or an anonymous donor, an egg from the woman or a donor, and in some cases surrogacy. In those instances where both individuals of a couple are infertile or the prospective father has non-functional sperm, one might envision using cloning of one member of the couple's nuclei to produce a child.

Although this constitutes an extension of current clinical practice, aside from the serious, moral and ethical issues surrounding this approach, there are significant technical and medical causes for caution, some of which were described in the research questions enumerated above.

In most situations of assisted reproduction, other than the intentional union of the gametes by in vitro techniques, the fertilized egg and initial cells of the early embryo are not otherwise manipulated. In some rare cases, such as preimplantation genetic diagnosis, the embryo is manipulated by the removal of one of the identical cells of the blastomere to test its genetic status. In contrast, if nuclear transfer were to be used as a reproductive option, it would entail substantially more invasive manipulation. Thus far, the animal cloning of Dolly is a singular success, one seemingly normal animal produced from 277 nuclear transfers. Until the experiment is replicated the efficiency, and even the validity, of the procedure cannot be fully determined. It is likely that the mere act of manipulating a nucleus and transferring it into an egg could decrease the percentage of eggs that go on to develop and implant normally, as well as increase the rate of birth defects.

Cloning and Genetic Determinism

The announcement of Dolly sparked widespread speculation about a human child being

1 created using somatic cell nuclear transfer. Much of the perceived fear that greeted this
2 announcement centered around the misperception that a child or many children could be
3 produced who would be identical to an already existing person.

4 This fear reflects an erroneous belief that a person's genes bear a simple relationship to
5 the physical and psychological traits that compose that individual. This belief, that genes alone
6 determine all aspects of an individual, is called "genetic determinism." Although genes play an
7 essential role in the formation of physical and behavioral characteristics, each individual is, in
8 fact, the result of a complex interaction between his or her genes and the environment within
9 which they develop. As social and biological beings we are creatures of our biological, physical,
10 social, political, historical, and psychological environments. Indeed, the great lesson of modern
11 molecular genetics is the profound complexity of both gene-gene interactions and gene-
12 environment interactions in the determination of whether a specific trait or characteristic is
13 expressed. In other words, there will never be another you.

14 While the concept of complete genetic determinism is wrong and overly simplistic, genes
15 do play a major role in determining biological characteristics including a predisposition to certain
16 diseases. Moreover, the existence of families in which many members are affected by these
17 diseases suggest that there is a single gene that is passed down with each generation that causes
18 the disease. When such a disease gene is identified, scientists often say they have "cloned the
19 gene for" breast cancer for instance, implying a direct cause and effect of gene and disease.
20 Indeed, the recent efforts of the Human Genome Project have led to the isolation of a large
21 number of genes that are mutated in specific diseases, such as Duchenne Muscular Dystrophy,
22 and certain types of breast and colon cancer.

23 However, recent scientific findings have revealed that a "one-gene, one-disease"
24 approach is far too simplistic. Even in the relatively small list of genes currently associated with
25 a specific disease, knowing the complete DNA sequence of the gene does not allow a scientist to
26 predict if a given person will get the disease. For example, in breast cancer there can be many
27 different changes in the DNA, and for some specific mutations there is a calculated risk of
28 developing the disease, while for other changes the risk is unknown. Even when a specific
29 genetic change is identified that "causes" the disease in some people, others may be found who
30 have the same change but do not get the disease. This is because other factors, either genetic or
31 environmental, are altered that mask or compensate for "the" disease gene. Thus even with the
32 most sophisticated understanding of genes, one cannot determine with certainty what will happen
33 to a given person with a single change in a single gene.

34 Once again, the reason rigid genetic determinism is false is that genes interact with each
35 other and with the environment in extremely complex ways. For example, the likelihood of
36 developing colon cancer, a disease with a strong hereditary component and for which researchers
37 have identified a single "causative" gene, is also strongly influenced by diet. When one considers
38 a human trait that is determined by multiple genes, the situation becomes even more complex.

1 The number of interactions between genes and environment increases dramatically. In fact, the
2 ability to predict what a person will be like knowing only their genes becomes virtually
3 impossible because it is not possible to know how the environment and chance factors will
4 influence the outcome.

5 Thus the idea that one could make through somatic cell nuclear transfer a team of
6 Michael Jordans, a physics department of Albert Einsteins, or an opera chorus of Pavarottis, is
7 simply false. Knowing the complete genetic makeup of an individual would not tell you what
8 kind of person that individual would become. Even identical twins who grow up together and
9 thus share the same genes and a similar home environment have different likes and dislikes, and
10 can have very different talents. The increasingly sophisticated studies coming out of human
11 genetics research are showing that the better we understand gene function, the less likely it is we
12 will ever be able to produce at will a person with any given complex trait.

13 Conclusions

14 The term "clone" has many meanings but in its simplest and most scientific sense it
15 means the making of identical copies of molecules, cells, tissues, and even entire animals. The
16 latest news about cloning Dolly the sheep involved somatic cell nuclear transplant cloning. In
17 this process the nucleus from an adult somatic cell is transplanted into an enucleated ovum to
18 produce a developing animal that is a "delayed" genetic twin of the adult.

19 There are many applications that nuclear transfer cloning might have for biotechnology,
20 livestock production, and new medical approaches. Work with embryonic stem cells and genetic
21 manipulation of early embryos in animal species (including nuclear transfer) is already providing
22 unparalleled insights into fundamental biological processes and promises to provide great
23 practical benefit in terms of improved livestock, improved means of producing pharmaceutical
24 proteins, and prospects for regeneration and repair of human tissues.

25 However, the possibility of using human cloning for the purposes of creating a new
26 individual entails significant scientific uncertainty and medical risk at this time. Potential risks
27 include those known to be associated with the manipulation of nuclei and eggs and those yet
28 unknown, such as the effects of aging, somatic mutation, and improper imprinting. These effects
29 could result in high rates of failed attempts at pregnancy as well as the increased likelihood of
30 developmentally and genetically abnormal embryos.

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Chapter Three

RELIGIOUS PERSPECTIVES

Over the last twenty-five years religious thinkers have discussed the prospect of human cloning in the context of long-standing religious traditions that often influence and guide citizens' responses to new technologies. Religious positions on human cloning are pluralistic in their premises, modes of argument, and conclusions about human cloning. Nevertheless, several major themes are prominent in Jewish, Roman Catholic, Protestant, and Islamic positions, including responsible human dominion over nature, human dignity and destiny, procreation, and family life. Some religious thinkers argue that cloning a human to create a child would be intrinsically immoral and thus could never be morally justified; they usually propose a ban on such human cloning. Some other religious thinkers contend that human cloning to create a child could be morally justified under some circumstances but hold that it should be strictly regulated in order to prevent abuses.

* * * * *

Media reports often depict the debate over the prospects of cloning humans as a classical confrontation between science and religion. This depiction is misleading: Not all arguments against cloning humans are religious, and not all religious thinkers oppose the cloning of humans in all circumstances. Furthermore, many contend that the possibility of cloning humans offers an opportunity for substantive dialogue between scientists and theologians. Probing the intersections of ethics, science, and theology can offer mutual enrichment. Scientists can see how research in genetics and biology raises theological questions, while theologians can consider whether and how religious convictions can accommodate new scientific knowledge (Gustafson, 1994). Therefore, the Commission sought to determine the positions on human cloning via somatic cell nuclear transfer held by a variety of religious thinkers and the arguments they offer to support their positions. The Commission was interested in religious arguments and conclusions about human cloning because religious traditions influence and guide many citizens' responses to various issues in biomedicine, including such novel developments as human cloning.

For purposes of recommending public policy in a democratic society, the Commission was also interested in the extent to which moral arguments in various religious traditions rest on premises accessible to others outside those traditions. Sometimes religious thinkers appeal to categories such as "nature," "reason," "basic human values," and "family values" that may speak to citizens outside their traditions because these categories do not necessarily depend solely on particular faith commitments, scripture, revelation, or religious authority. ~~This more secular~~ *Such categories of* discussion may therefore contribute to a broader societal discussion of the ethical arguments for

1 and against cloning humans, which are examined further in the following chapter. Indeed,
2 NBAC was interested in determining whether various religious traditions and secular approaches
3 achieve a rough consensus about appropriate public policy toward creating children through
4 somatic cell nuclear transfer at this time.

5 Finally, the views of a wide range of communities, including religious communities, are
6 important in determining whether policies under consideration are feasible and whether their
7 social benefits outweigh their social costs. For example, a particular policy may not be feasible,
8 and may even be counterproductive, if it engenders vigorous, widespread, and sustained moral
9 objection.

10 NBAC solicited oral and written presentations from scholars in several religious
11 traditions, contracted for a scholarly analysis of the views of these and other religious traditions,¹
12 and received public testimony and written submissions from various other individuals and groups
13 with religious orientations. What follows builds on these materials and presents some of the key
14 themes in several western religious interpretations and evaluations of cloning humans. This
15 chapter is presented in the spirit of sustaining a national dialogue but also in complete awareness
16 that the Commission may not have fully understood the traditions described. (This chapter
17 concentrates on Jewish, Roman Catholic, Protestant, and Islamic views; a discussion of other
18 religious views appears in the commissioned paper by Courtney Campbell.)

19 Religion and Human Cloning: An Historical Overview

20 It is possible to identify four recent overlapping periods in which theologians and other
21 religious thinkers have considered the scientific prospects and ethics of the cloning of humans.
22 The first phase, which began in the mid-1960s and continued into the early 1970s, was shaped by
23 a context of expanded choices and control of reproduction (e.g., the availability of the birth
24 control pill), the prospects of alternative, technologically assisted reproduction (e.g., *in vitro*
25 fertilization [IVF]), and the advocacy by some biologists and geneticists of cloning "preferred"
26 genotypes, which, in their view, would avoid overloading the human gene pool with genes that
27 are linked to deleterious outcomes and that could place the survival of the human species at risk.

28 Several prominent theologians engaged in these initial discussions of human genetic
29 manipulation and cloning, including Charles Curran, Bernard Häering, Richard McCormick, and
30 Karl Rahner within Roman Catholicism, and Joseph Fletcher and Paul Ramsey within
31 Protestantism. The diametrically opposed positions staked out by the last two theologians gave
32 an early signal of the wide range of views that are still expressed by religious thinkers.

¹ Much of the material in this chapter is derived from a commissioned paper prepared for the National Bioethics Advisory Commission by Courtney S. Campbell, Department of Philosophy, Oregon State University, titled "Religious Perspectives on Human Cloning."

1 Joseph Fletcher advocated expansion of human freedom and control over human
2 reproduction. He portrayed the cloning of humans as one of many present and prospective
3 reproductive options that could be ethically justified by societal benefit. Indeed, for Fletcher, as
4 a method of reproduction, cloning was preferable to the "genetic roulette" of sexual reproduction.
5 He viewed laboratory reproduction as "radically human" because it is deliberate, designed,
6 chosen, and willed (Fletcher, 1971; 1972; 1974; 1979).

7 By contrast, Paul Ramsey portrayed the cloning of humans as a "borderline" or moral
8 boundary that could be crossed only at risk of compromise to humanity and to basic concepts of
9 human procreation. Cloning threatened three "horizontal" (person-person) and two "vertical"
10 (person-God) border-crossings. First, clonal reproduction would require directed or managed
11 breeding to serve the scientific ends of a controlled gene pool. Second, it would involve non-
12 therapeutic experimentation on the unborn. Third, it would assault the meaning of parenthood by
13 transforming "procreation" into "reproduction" and by severing the unitive end (expressing and
14 sustaining mutual love) and the procreative end of human sexual expression. Fourth, the cloning
15 of humans would express the sin of pride or hubris. Fifth, it could also be considered a sin of
16 self-creation as humans aspire to become a "man-God" (Ramsey, 1966; 1970).

17 A second era of theological reflection on cloning humans began in 1978, a year that was
18 notable for two events, the birth in Britain of the first IVF baby, Louise Brown, and the
19 publication of David Rorvik's *In His Image*, an account alleging (falsely) the creation of the first
20 cloned human being (Rorvik, 1978). Christian theologians concentrated more on the ethical
21 issues raised by IVF, while Jewish scholars, such as Seymour Siegel and Fred Rosner, also
22 directed attention to cloning humans, and were neither as supportive as Fletcher nor as critical as
23 Ramsey. They instead indicated the need for more extensive discussion of this topic within the
24 Jewish community.

25 This period also witnessed the beginning of formal ecclesiastical involvement with
26 questions of genetic manipulation. In 1977 the United Church of Christ produced a study
27 booklet on "Genetic Manipulation," which appears to be the earliest reference to human cloning
28 among Protestant denominational literature (Lynn, 1977). It provided a general overview of the
29 science and ethics of cloning humans but stopped short of a specific theological verdict.

30 Protestant-organized ecumenical bodies such as the World Council of Churches (1975,
31 1982, 1989) and the National Council of Churches of Christ (1980, 1983, 1986), as well as some
32 individual denominations, issued resolutions or position statements that cautiously endorsed
33 genetic interventions for therapeutic purposes. In addition, in 1979, concerns about genetic
34 engineering expressed by Jewish, Protestant, and Roman Catholic leaders led President Jimmy
35 Carter to ask the President's Commission for the Study of Ethical Problems in Medicine and
36 Biomedical and Behavioral Research to examine the scientific, ethical, and social issues of gene
37 splicing (President's Commission, 1982). The President's Commission addressed the aspects of
38 "genetic engineering" that use recombinant DNA technology to treat disease, but it did not

1 address other procedures often encompassed by the phrase, such as IVF or cloning organisms.

2 The discussions of the 1970s continued into the 1980s with particular attention to IVF,
3 artificial insemination by donor, and surrogacy. These techniques challenged traditional notions
4 of the family by separating genetic and rearing fatherhood and genetic, gestational, and rearing
5 motherhood, as well as raising questions about whether the contractual and commercial ties in
6 many of these arrangements were inimical to traditional religious views of the family.

7 A third era of religious discussion began in 1993 with the report from George
8 Washington University of the separation of cells in human blastomeres to create multiple,
9 genetically identical embryos. The Roman Catholic Church expressed vigorous opposition to the
10 procedure, and a Vatican editorial denounced the research as "intrinsically perverse." Catholic
11 moral theologians invoked norms of individuality, dignity, and wholeness in condemning this
12 research (McCormick, 1993; 1994; Shannon, 1994). While many Conservative Protestant
13 scholars held that this research contravened basic notions of personhood such as freedom, the
14 sanctity of life, and the image of God, some other Protestant scholars noted its potential medical
15 benefits and advocated careful regulation rather than prohibition.

16 The fourth and most recent stage of religious discussion has come in the wake of the
17 successful cloning of Dolly the sheep through the somatic cell nuclear transfer technique, as the
18 cloning of a human once again appeared to be a near-term possibility. Several Roman Catholic
19 and Protestant thinkers have reiterated and reinforced past opposition and warnings. For
20 example, Protestant theologian Allen Verhey drew on the arguments initially voiced by Paul
21 Ramsey in concluding that an account of the good life in a family is "inhospitable" to the cloning
22 of humans (Verhey, 1994;1997).

23
24 However, some Protestant thinkers, in reflecting on the meaning of human partnership
25 with ongoing divine creative activity, have expressed qualified support for cloning research and
26 for creating children using somatic cell nuclear transfer techniques. Likewise some Jewish and
27 Islamic thinkers encourage continuing laboratory research on animal models and even laboratory
28 work on the possibility of cloning human beings (only in pursuit of a worthy objective), while
29 expressing deep moral reservations, at least at this time, about the transfer of a human embryo
30 obtained by nuclear transfer techniques to a womb for purposes of gestation and birth.
31 Testimony presented to NBAC in public hearings on March 13 and 14, 1997, provides some of
32 the earliest theological statements in this renewed discussion of the ethics of cloning research and
33 of cloning humans.

34 Several conclusions emerge from this brief historical overview:

- 35 • Over the past twenty-five years, theologians have engaged in repeated discussions of the
36 prospect of cloning humans that anticipate and illuminate much current religious
37 discussion of this topic.

- 1 • Theological and ecclesiastical positions on cloning humans are pluralistic in their
2 premises, their modes of argument, and even their conclusions. In short, they exhibit the
3 pluralism characteristic of American religiosity.
- 4 • The religious discussion of cloning humans has connected it closely with on-going
5 debates about technologically-assisted reproduction and genetic interventions.
- 6 • Despite changes in scientific research and technical capability, the values that underlie
7 religious concerns about cloning humans have endured and continue to inform public
8 debate.

9 **Themes in Theological Bioethics**

10 This section, without any pretense of comprehensiveness, examines several major,
11 overlapping themes in Western faith traditions that bear on positions taken on the cloning of
12 humans. It considers both broad religious convictions and moral norms. These traditions have
13 articulated a variety of ethical norms to address a wide range of practical issues and problems.
14 These norms may be derived from sacred writings, traditions of interpretation, reason, and
15 personal experience, among other sources, and they can be applied to the wide array of moral
16 choices people confront from the beginning to the end of life.

17 **The Biblical Account of the Creation of Humans**

18 The question of personhood or human distinctiveness is commonly described and
19 explained in Judaism and Christianity with reference to the theological theme of creation in the
20 image of God. Interpretations of the moral meaning of the image of God depend on prior
21 convictions about the nature of God and the characteristics of God that human beings are
22 believed to reflect. The biblical story of creation is most commonly used for interpreting the
23 image of God. Particularly significant is the language of Genesis, chapter 1, verses 27-28: "So
24 God created man in his own image, in the image of God he created him, male and female he
25 created them. And God blessed them, and God said to them, 'Be fruitful and multiply, and fill
26 the earth and subdue it; and have dominion over the fish of the sea and over the birds of the air
27 and over every living thing that moves upon the earth'" (Revised Standard Version).

28 Several characteristics of humanity have been inferred and explicated from the biblical
29 story of creation:

- 30 • Human beings as created in God's image receive the gift of freedom and moral agency.
31 Moral agency is inherent in the human self and creates moral responsibilities that include
32 respect for the equal freedom and agency of other persons. The moral correlate of
33 personal freedom is personal responsibility for actions before one's conscience, others,

and ultimately God.

- Humans are fundamentally equal because they are all created in God's image. Their fundamental equality transcends any differentiation based on gender, race, class, or ethnicity.
- Human beings are also relational and social creatures. They are created in and for relationships with God and for community with other persons as well as the rest of creation.
- The image of God is reflected in human diversity, including but not limited to gender diversity. The differentiation of the sexes represents the divine warrant for procreation as well as a positive evaluation of sexuality.
- Human beings are embodied selves. The person is revealed and experienced through the body, not merely as an intellectual or spiritual essence, or as a disembodied mind or will.
- Although human beings are in nature, they also transcend nature, and they express the image of God through the exercise of their creative capacities and potential, including their "dominion" over the natural world.
- Although human beings are created in God's image, they are not God. They are finite and fallible, with limited capacities to predict and direct the course of actions they initiate, or to assess accurately the outcomes of these actions.

Each of these features of the image of God helps explain religious responses to the prospects of creating a child through human cloning. Nevertheless, different religious traditions and strands within those traditions interpret and weight these features and their implications somewhat differently, particularly in relation to the divine commands that follow the creation of humans in God's image. These different views of humans as created in the image of God, with certain responsibilities, are reflected in major religious themes regarding the cloning of humans: responsible human dominion over nature; human dignity; and procreation and families.

Responsible Human Dominion Over Nature

Warnings Not to Play God. As often happens when a powerful new scientific tool is developed, the announcement that mammalian somatic cell nuclear transfer cloning was possible generated strong warnings against "playing God." This slogan is usually invoked as a moral stop sign to some scientific research or medical practice on the basis of one or more of the following distinctions between human beings and God:

- Human beings should not probe the fundamental secrets or mysteries of life, which

1 belong to God.

- 2 • Human beings lack the authority to make certain decisions about the beginning or ending
3 of life. Such decisions are reserved to divine sovereignty.
- 4 • Human beings are fallible and also tend to evaluate actions according to their narrow,
5 partial, and frequently self-interested perspectives.
- 6 • Human beings do not have the knowledge, especially knowledge of outcomes of actions,
7 attributed to divine omniscience.
- 8 • Human beings do not have the power to control the outcomes of actions or processes that
9 is a mark of divine omnipotence.

10 The warning against “playing God” serves to remind human beings of their finiteness and
11 fallibility. By not recognizing appropriate limits and constraints on scientific aspirations,
12 humans reenact the Promethean assertion of pride or hubris. In the initial theological discussions
13 of cloning humans, Ramsey summarized his objections by asserting: “Men ought not to play God
14 before they learn to be men, and after they have learned to be men, they will not play God”
15 (Ramsey, 1970, p.138).

16 Even within religious communities, however, the warning against “playing God” may not
17 be considered a sufficient argument against human cloning. Allen Verhey contends that this
18 warning is simply too indiscriminate to provide ethical guidance. Furthermore, it overlooks
19 moral invitations to play God, particularly in the realm of genetics (Verhey, 1995). While
20 agreeing with Ramsey that human beings are not called to “play God,” Protestant Ted Peters
21 argues that this does not by itself define what is necessary for us to be human. Hence, we are
22 responsible for using our creativity and freedom (features of the image of God) to forge a destiny
23 more consonant with human dignity. In “playing human,” Peters contends, there is no
24 theological reason to leave human nature unchanged, and no theological principles that the
25 cloning of humans necessarily violates (Peters, 1997).

26 The Quest for Knowledge. For major strands of Christian, Jewish, and Islamic traditions,
27 the quest for scientific knowledge is not, in general, theologically problematic or threatening.
28 Islamic scholars, for example, emphasize that all scientific discovery is ultimately a revelation of
29 the divinely ordained creation. Scientific knowledge is thereby a symbol or sign of God's
30 creation (Hathout, 1997). Along these lines, Sheikh Fadlallah, a Shi'ite Muslim jurist,
31 commented that the recent cloning discovery occurred “because God allowed it” (Fadlallah,
32 1997), and Abdulaziz Sachedina, an Islamic scholar, observed that cloning may be a divinely
33 given opportunity for human moral training and maturation (Sachedina, 1997). Positive general
34 assessments of scientific inquiry also appear in Protestant, Catholic, and Jewish traditions. One
35 ecclesiastical statement in the Calvinist tradition, which views the world as a theater of God's

glory, suggests that “in the sciences, the human does indeed receive glimpses of God's theater” (Reformed Church in America, 1988).

The prospects for dialogue and agreement between religion and science can dissipate in the context of specific scientific applications. For the religious traditions under consideration, scientific descriptions of the world, however important, do not supply theological interpretations or provide the moral standards for acting in the world. Instead, these traditions insist that two principal questions—who controls technological developments, and what are the ends and purposes of technology—are ethical rather than scientific or technical. Thus, these traditions generally endorse the scientific quest for knowledge, while at the same time sharply criticizing and even rejecting particular applications of scientific discoveries, just as many thinkers within these traditions do with respect to the prospect of cloning humans to create children. Some religious thinkers also take pains to distinguish their reservations about cloning humans from their response to genetic research in general (Duff, 1997).

Finally, while generally supporting science, many religious thinkers criticize what they perceive to be a “technological imperative,” frequently propelled by commercial forces, to pursue such projects as the cloning of humans when they appear to be possible and/or potentially profitable without giving sufficient attention to the risks involved (Cahill, 1997, p. 5). Still others insist that, however valuable, scientific “progress” remains an optional goal for the society and its individual members, who should not transgress important moral and human limits in its pursuit (Meilaender, 1997, p. 6).

Responsible Dominion. Religious traditions variously interpret the biblical mandate of human dominion over nature. Three different interpretations are particularly significant in debates about cloning humans. One common model is an ethic of stewardship, which holds that humans are entrusted with administrative responsibility for creation. Human stewardship involves caring for and cultivating creation after the manner of a gardener. This stewardship ethic, one version of which is prominent in Roman Catholicism, accepts nature as a good to be maintained and preserved.

A second model suggests a “partnership” between human beings and God in caring for and improving upon creation. Rabbi Dorff (1997, pp. 6-7) notes that “we are God’s ‘partners in the ongoing act of creation’ when we improve the human lot in life.” The Jewish tradition emphasizes that God has given humans a “positive commandment” to “master the world” (Tendler, 1997), and some Jewish thinkers explicate human mastery over nature by reference to the two directions for Adam and Eve in the Garden: They were “to work it [the garden] and to preserve it” (*Genesis* 2:15). To “work” nature is to improve it to meet human needs, and this activity is both right and obligatory “as long as we preserve nature” (Dorff, 1997, p. 6). It also includes efforts to heal. Human responsibility, in the final analysis, involves “balancing” human and divine actions in this partnership (Dorff, 1997).

1 This second model also appears in some Islamic thought. One Islamic scholar stresses
2 that “as participants in the act of creating with God, human beings can actively engage in
3 furthering the overall well-being of humanity by intervening in the works of nature, including the
4 early stages of embryonic development, to improve human health” (Sachedina, testimony 1997).
5 The natural world on this second model is inherently malleable and can be shaped in several
6 different ways in service of valuable human and divine goals. Proponents of this model could
7 view cloning research, and perhaps even cloning humans in some circumstances, as using human
8 creative potential for good.

9 A third perspective, which some Protestants defend, is potentially even more receptive to
10 the prospect of cloning humans. It understands human beings as “created co-creators.” On the
11 one hand, human beings are created, dependent on God, and finite and fallible. On the other
12 hand, they assume the role of co-creator to acquire and implement knowledge to improve
13 humanity and the world. Human beings are called to “play human” (Peters, 1997) through their
14 freedom and responsibility in creating an essentially open human future. Reproductive and
15 genetic technologies, along with technologies to create a child through cloning, can express
16 responsible created co-creatorship.

17 Although Genesis notes that creation is “good” and humanity “very good,” humans have
18 displayed, according to some traditions, an irremediable propensity to use their divinely
19 authorized dominion for unauthorized domination, to violate their covenant of partnership with
20 God, and to create after their own image rather than the divine image. The person created in the
21 image of God is thus also marked by a tendency to transgress limits, to commit what some
22 traditions call sin. As a consequence, all human activities are pervasively imperfect. The
23 narratives in Genesis of Adam and Eve in the Garden of Eden, their eating of the fruit of the Tree
24 of the Knowledge of Good and Evil, and the later Tower of Babel often appear in religious
25 discussions of human temptations and tendencies to transgress appropriate limits (see, for
26 example, Tendler, 1997, and Dorff, 1997).

27 The prospect that humans can and will choose evil rather than good dictates caution as a
28 moral necessity (Gustafson, 1994; Duff, 1997, p.2). Even though human imperfection does not
29 necessarily justify halting technological advances, it should, according to many religious
30 thinkers, evoke modesty about human aspirations and achievements (Hefner, 1997).

31 Human Destiny. Theological views of medicine and medical interventions grounded in
32 themes of creation may be somewhat conservative with respect to reproductive or genetic
33 technologies, not to mention cloning, because of the divine evaluation of nature, including
34 human beings, as good. For instance, the goal of medicine may be conceived as that of restoring
35 disordered biological organisms to their initial goodness, rather than improving them. By
36 contrast, theological positions that focus on human destiny rather than nature can sometimes
37 support an array of reproductive and genetic interventions as ways to improve the human
38 condition.

1 The question of human destiny has been an underlying theme in the debate about cloning
2 humans from its inception. Several decades ago scientific proponents such as Muller and
3 Lederberg were pessimistic about the survival of the species because of genetic overload.
4 Cloning represented a prospective intervention to avoid this "genetic apocalypse" and promised a
5 future of unlimited possibility. Paul Ramsey's theology of cloning likewise assumed an
6 apocalyptic prognosis of human destiny, though very different in content: "Religious people have
7 never denied, indeed they affirm, that God means to kill us all in the end, and in the end he is
8 going to succeed" (Ramsey, 1970, p. 136). The end of species survival did not, for Ramsey,
9 justify the means of cloning. Survival is meaningful only if values of human dignity and freedom
10 are respected.

11 The use of cloning to save the endangered human species is no longer part of the debate,
12 although cloning techniques have received some support to rescue endangered animal species.
13 However, the general question of the extent to which human beings are shapers and creators of
14 their personal and collective futures continues to be important and contested. Some theologians
15 in the debate about cloning humans reject a rigid and static conception of human nature and
16 destiny in favor of a conception that is more open. This more open conception reflects an image
17 of a creative God and a dynamic view of history. The specific theological-ethical interpretation
18 of cloning humans then turns on the nature of human responsibility in the face of uncertain, and
19 perhaps unforeseeable, outcomes.

20 Some Jewish thinkers affirm that the divine mandate of mastery empowers human beings
21 with the responsibility to shape a malleable world through discovery and innovation. They stress
22 that the Jewish tradition is relatively optimistic because of divine control and care in the face of
23 uncertainty about unanticipated consequences. Indeed, to be overly cautious to the point of
24 moral paralysis may invite trouble. As one Orthodox rabbi has expressed it: "Human beings do
25 the best that they can. If our best cost/benefit analysis says go ahead, we go ahead. "G-d protects
26 the simple" is a Talmudic principle that allows us to assume that when we do our best G-d will
27 take care of what we could not foresee or anticipate. If things do not work out, the theological
28 question is G-d's to answer; not ours" (Freundel, 1994; 1997). On this view, cloning humans
29 could express moral responsibility insofar as it is directed to the service of God and humanity.
30 Furthermore, some affirm, "children are our destiny" (Dorff, 1997, p. 11).

31 Often Jewish thinkers also emphasize the moral education of progeny who will live in the
32 generations to come. One form of immortality discussed in rabbinic sources comes through the
33 influence of parents (and others) on their children. The generations are bound together in part by
34 the ongoing obligations of transmitting knowledge and skills and by teaching and developing
35 moral dispositions. Rabbi Tendler emphasizes the importance of moral education as the best
36 form of human control over cloning technology: "Are we good enough to handle this good
37 technology? Of course we are, if we can set limits on it. And when we can train a generation of
38 children not to murder or steal, we can prepare them not to use this technology to the detriment
39 of mankind" (Tendler, 1997).

1 Some Protestants emphasize the idea of "continuing creation," coupled with the theme
2 that persons are co-creators who are called to participate with God in shaping a better future.
3 Indeed, human destiny is so open and indefinite that the Christian may be a "co-explorer" with
4 God in discovering new and unlimited possibilities through innovative technologies (Cole-
5 Turner, 1987). This perspective on human destiny can offer qualified support to human cloning,
6 insofar as it is technically feasible and publicly supported.

7 These theological accounts of human destiny do not simply bless and anoint scientific
8 progress, because they are balanced, within each tradition, by repeated warnings, often in
9 narrative form, about not crossing certain lines or boundaries. The archetypal figure is
10 Prometheus in Greek mythology, but religious traditions have their own Promethean analogues.
11 The theological caveat is that creative initiative may be a form of rebellion of the created against
12 the creator. The consequences of such rebellion may include catastrophic havoc and perhaps
13 even destruction of the human creator or of what has been created. This lesson is as fundamental
14 to religious narrative as it is to modern science fiction. The task for religious traditions is to
15 identify what lines may not be crossed and to determine whether cloning a human to create a
16 child is one such line. Much of the debate about limits focuses on human dignity and several
17 related concepts.

18 **Human Dignity**

19 It has been argued that the most significant issue genetic science forces on society
20 concerns the understanding of human nature (Gustafson, 1992). This same issue emerges in
21 theological discourse on the cloning of humans. Lutheran theologian Philip Hefner argues that
22 cloning is a "revelation of the human situation.... In cloning, we are, in fact, addressing ourselves,
23 and it is about ourselves that we have the greatest questions" (Hefner, 1997). One major theme
24 in the theological conception of creation in God's image is human dignity: Humans have dignity
25 because they are created in God's image.

26 Appeals to human dignity are prominent in Roman Catholic analyses and assessments of
27 the prospects of human cloning, which base "human dignity" on the creation story and on the
28 Christian account of God's redemption of human beings. The Catholic moral tradition views the
29 cloning of a human being as "a violation of human dignity" (Haas letter, 1997; see also Pope
30 John Center, 1997). Concerns about human dignity also appear in religious perspectives that are
31 more receptive to the possibility of human cloning; these concerns emerge in the moral limits or
32 conditions they set for human cloning. Even when the language of human dignity is not used,
33 arguments for and specifications of the rights of persons created through cloning often represent
34 what others include under the phrase "human dignity." And when the language of human dignity
35 is used, it is often specified in more concrete concepts and norms, such as human equality and the
36 sanctity of life.

37 Religious thinkers generally do not question whether a person created through cloning is

1 a human being created in God's image. They extend to persons created through cloning the
2 same moral protections that already apply to other persons created in the image of God. For
3 instance, Rabbi Elliot Dorff argues that "[n]o clone may . . . legitimately be denied any of the
4 rights and protections extended to any other child" (Dorff, 1997, p. 5). However, many fear that
5 the human dignity of persons created through cloning will be violated by the denial of such rights
6 and protections, for instance, through enslavement to others and other forms of "man's mastery
7 over man" (Tendler, 1997).

8 Human cloning would violate human dignity, according to some religious opponents,
9 because it would "jeopardize the personal and unique identity of the clone (or clones) as well as
10 the person whose genome was thus duplicated" (Pope John Center, 1997). This problem does
11 not arise in the case of identical twins, because neither is the "source or maker of the other"
12 (Pope John Center, 1997). Religious concerns about identity and individuality focus mainly on
13 how persons created through cloning will inevitably or possibly be treated, rather than whether
14 such persons are actually unique creatures in God's image. Rejecting genetic determinism,
15 religious thinkers hold that cloning humans would "produce independent human beings with
16 histories and influences all their own and with their own free will" (Dorff, 1997, p. 6). The
17 person created through cloning will be "a new person," an integrated body and mind, with unique
18 experiences." However, it will doubtless be harder for such persons "to establish their own
19 identity and for their creators to acknowledge and respect it" (Dorff, 1997, p. 6). Even for
20 absolute opponents, the process of cloning humans only violates human dignity; it does not
21 diminish human dignity: "In the cloning of humans there is an affront to human dignity. . . . Yet,
22 in no way is the human dignity of that person [the one who results from cloning] diminished"
23 (Pope John Center, 1997, p. 3).

24 Sanctity of life is one norm associated with human dignity. For instance, the prohibition
25 of the shedding of human blood is connected with God's creation of humans in his own image
26 (Genesis 9:6). Opponents often view the cloning of a human as a breach, or at least as a potential
27 breach, of the sanctity of life. In rejecting human cloning, Joseph Cardinal Ratzinger of the
28 Vatican insisted that "the sanctity of [human] life is untouchable" (quoted in Pope John Center,
29 1997, p. 2). Even those who offer limited support for human cloning, in part on the grounds that
30 it could be used in support of life, argue that it is necessary to set conditions and limits in order to
31 prevent harm to persons who are created through cloning. Not only do they rule out such
32 egregious violations of the sanctity of life as sacrificing persons created through cloning in order
33 to obtain their organs for transplantation, they also worry about what will be done with the "bad
34 results," that is, the "mistakes" that will be inevitable at least in the short term (Dorff, 1997, p. 3-
35 4). In addition, most recognize that the risks to persons created through cloning are now so
36 unknown and would virtually rule out human cloning for the present, those who create clones
37 could not be sure that they are "doing no evil" (Tendler, 1997).

38 Objectification also represents a fundamental breach of human dignity. To treat persons
39 who are the sources of genetic material for cloning or persons who are created through cloning as

mere objects, means or instruments violates the religious principle of human dignity as well as the secular principle of respect for persons. Cloning humans would necessarily involve objectification, some religious thinkers argue, because it would treat the child as "an object of manipulation" by potentially eliminating the marital act and by attempting "to design and control the very identity of the child" (Pope John Center, 1997). Cloning humans is wrong, in short, because "it subjects human individuals at their most vulnerable, at their very coming-into-being, to the arbitrary whim, power and manipulation of others" (Haas, letter, 1997). For other religious thinkers who accept human cloning under some circumstances, it is necessary to reduce the effects of objectification, for example, by a commitment to accept and care for the "mistakes" made in cloning (Dorff, 1997).

Objectification can become commodification when commercial and economic forces determine whether and how a person is treated as an object. Religious opponents of human cloning stress that objectification through commodification is a major risk and worry that "economic incentives will control when humans will be cloned" (Cahill, 1997, p. 3). Commodification would deny "the sacred character of human life depicted in the Jewish tradition, transforming it instead to fungible commodities on the human marketplace to be judged by a given person's worth to others" (Dorff, 1997, p. 2).

Religious thinkers note that the process of ^{children through cloning} human cloning would or could violate the human dignity of agents, that is, those who create ~~the clone~~, as well as those who are created through cloning. The concepts and norms associated with human dignity cannot be reduced to secular ideas of autonomy, even though they may overlap to some extent. Human dignity sets more limits than autonomy does on what the agent may do. Even though Protestants are often pictured as "stout defenders of human freedom," as one Protestant theologian notes, "they have not located the dignity of human beings in a self-modifying freedom that knows no limit..." (Meilaender, 1997, p. 6). Likewise, a Roman Catholic statement insists that "there is an affront to human dignity for the ones who actively participate in the process as well as for the one who results from the cloning" (Pope John Center, 1997, p. 3).

Whether creating a human being through cloning necessarily or only under certain circumstances violates human dignity depends on the conception of rights and duties that specify human dignity. For instance, some religious thinkers argue that human cloning would violate inherent human dignity "by exceeding the limits of delegated dominion," a topic that was discussed above (Pope John Center, 1997, p. 3; see also Haas, letter, 1997). The next section on Procreation and Families will explicate the claim, strongly associated with human dignity in Roman Catholic thought (as well as in some Protestant thought), that those coming into being have a fundamental "right to be engendered by the personal act of a man and a woman committed to one another and their future children in marriage" and not to be subjected to "impersonal manipulative actions which render them susceptible to being used, and thereby abused, by those manipulating them into being" (Haas, letter, 1997).

Procreation and Families

Procreation and Reproduction. In the initial phase of theological debate about cloning humans, Paul Ramsey argued that the covenant of marriage includes the goods of sexual love and procreation, which are divinely ordained and intrinsically related: Human beings have no authority to sever what God had joined together. On this basis, Ramsey, a Protestant, joined with several Roman Catholic moral theologians, such as Bernard Häring and Richard McCormick, in objecting to the cloning of humans as part of the panoply of reproductive technologies. They claimed that such technologies separate the unitive and procreative ends of human sexuality and transform "procreation," which at most puts humans in a role of co-creator, into "reproduction." The Vatican's 1987 Instruction on Respect for Human Life (Donum Vitae) rejected human cloning either as a scientific outcome or technical proposal: "Attempts or hypotheses for obtaining a human being without any connection with sexuality through 'twin fission,' cloning, or parthenogenesis are to be considered contrary to the moral law, since they are in opposition to the dignity both of human procreation and of the conjugal union" (Congregation for the Doctrine of the Faith, 1987).

A similar critique distinguishes "begetting" (procreating) from "making" (reproducing). According to the Nicene Creed of early Christianity, Jesus, as the authentic image of God and the normative exemplar of personhood, is "begotten, not made" of God. The theological interpretation of "begetting" emphasizes likeness, identity, equality; begetting expresses the parent's very being. By contrast, "making" refers to unlikeness, alienation, and subordination; it expresses the parent's will as a project.

Drawing out the implications of this distinction, Oliver O'Donovan, an Anglican theologian, portrays the cloning of humans as the culmination of scientific or technical "making" in human reproduction: "[T]he development of cloning techniques. . . will be a demonstration, if it occurs, that mankind does have the awesome technical power to exchange the humanity which God has given him for something else, to treat natural humanity itself as a raw material for constructing a form of life that is not natural humanity but is an artificial development out of humanity" (O'Donovan, 1984; see also Meilaender, 1997). Thus, this exercise of technological power would come at the cost of an artificial, diminished humanity. It would also disrupt the fundamental relational ties of likeness, identity, and equality. A child created through cloning is designed and manufactured as a product, rather than welcomed as a gift (Meilaender, 1997). Moreover, the process is itself inauthentic, or "fabricated," with respect to what it means to be human (Ramsey, 1970).

For some religious thinkers, this sharp distinction between begetting and making also challenges widely accepted reproductive technologies. For instance, Lutheran Gilbert Meilaender testified before NBAC that even though human cloning "marks a new and decisive turn," he "would have gotten off the train" of reproductive technology long before it reached cloning (Meilaender, 1997).

1 However, many religious thinkers do not accept the sharp separation between begetting
2 and making, because it could rule out various reproductive technologies that they find acceptable,
3 just as many do not accept the absolute connection between unitive and procreative meanings of
4 sexual acts, in part because it would rule out artificial contraception, which they find acceptable.
5 They may, nevertheless, still reject the cloning of humans to create children because they
6 perceive it to be radically different from all other methods of technologically-assisted
7 reproduction. Thus, they may stress the radically new features of human cloning, perhaps even
8 viewing it as a “genuine revolution” in reproduction.

9 Concerns about the Family. Religious traditions usually approach the cloning of humans
10 to create children from the standpoint of familial relationships and responsibilities rather than
11 from the standpoint of personal rights and individual autonomy. Hence, a primary moral
12 criterion is the impact of cloning humans on the integrity of the family, a concern that includes
13 but also goes beyond the inseparable goods of marriage and the primacy of begetting over
14 making.

15 The family has been valued as the prime social institution and, in some religious
16 traditions, a divinely ordained institution for the bearing and nurturing of children. Within
17 Roman Catholic moral teaching, procreation and education of offspring are requirements of
18 natural law. Paul Ramsey's opposition to the cloning of humans stemmed in part from a view
19 that Christians perform their primary responsibility to future generations through procreation and
20 care for children. Jewish law and Islamic law also impose fundamental duties and
21 responsibilities through spousal, parenting, and familial relationships, and through
22 intergenerational ties.

23 Protestant theologian Allen Verhey appeals to the concept of a “good life in a family” to
24 reject human cloning. He maintains that the primary justifications for human cloning—the
25 principle of freedom and the principle of utility—are necessary but insufficient guidelines for the
26 moral life of a family. In particular, Verhey focuses his critique on the potential disruption of the
27 parent-child relationship: The cloning of humans risks transforming children into “products” of
28 technological achievement rather than “gifts” created in love (Verhey, 1997). As products,
29 children become objects, and objectification violates what it means to treat a child as a gift.

30 Similarly, Lisa Cahill, a Roman Catholic moral theologian, argues that “the child who is
31 truly the child of a single parent is a genuine revolution in human history, and his or her advent
32 should be viewed with immense caution.” She further contends that cloning violates “the
33 essential reality of human family and ... the nature of the socially related individual within it. We
34 all take part of our identity, both material or biological and social, from combined ancestral
35 kinship networks. The existing practice of ‘donating’ gametes when the donors have no
36 intention to parent the resulting child is already an affront to this order of things. But, in such
37 cases, as in cases of adoption where the rearing of a child within its original combined-family
38 network is impossible or undesirable, the child can still in fact claim the dual-lineage origin that

characterizes every other human being. Whether socially recognized or not, this kind of ancestry is an important part of the human sense of self (as witnessed by searches for 'biological' parents and families), as well as a foundation of important human relationships." Cloning humans to create children, Cahill concludes, would constitute an "unprecedented rupture in those biological dimensions of embodied humanity which have been most important for social cooperation" (Cahill, testimony, 1997). At the extreme, cloning humans would not only free human reproduction from marital and male-female relationships, but would "allow for the emancipation of human reproduction from any relationship" (Mohler). Furthermore, echoing Cahill's concern about "intergenerational family networks," Protestant theologian Meilaender stresses that the cloning of humans "would symbolically represent an enormous shift in our understanding of the relation of the generations," and that this symbolic shift would have incalculably risky effects that should not be unleashed (Meilaender, letter, 1997).

Concerns about lineage and intergenerational relations in other religious traditions also set limits on or challenge the cloning of humans to create children. For example, Islamic scholar Abdulaziz Sachedina suggests that Islam could accept some therapeutic uses of human cloning "as long as the lineage of the child remains religiously unblemished" (Sachedina, 1997, pp. 6-7). And some Jewish thinkers worry that cloning humans may diminish the ethic of responsibility because of changed roles (father, mother, child) and relationships (spousal, parental, filial). It may be unclear who has what responsibilities to whom between and among the generations. According to Rabbi Tendler, "we do not live well with generational inversion" of the sort that human cloning could produce (Tendler, 1997). In particular, he stresses concerns about honoring parents and inheritance laws. However, cloning humans, for acceptable ends, may in some narrow respects be morally "easier" for the Jewish tradition, from the standpoint of its potential impact on the family, than reproductive technologies that use donor insemination or egg donation because it would not raise the same concerns about consanguineous relationships (Dorff, 1997; Tendler, 1997, both in transcript, pp. 78-79).

Even though concerns about family relationships dominate much of the religious discussion of human cloning, some religious thinkers challenge these concerns. For example, while giving "top priority" to children's interests in a religious-moral assessment of human cloning, and while noting "serious reasons" for reservations about research into human cloning, Protestant ethicist Nancy Duff argues that "the idea that it would undermine the relationships between men and women or the basic family unit is not . . . morally or theologically convincing" (Duff, 1977, p. 11).

Assessments of Acts and Public Policies

Religious thinkers and traditions often provide moral guidance to participants in their own communities. As a result, they direct many of the themes, norms, and arguments presented in this chapter primarily to those within particular faith traditions. However, religious thinkers and communities also frequently address the larger society, sometimes even proposing specific

public policies in addition to trying to alter cultural beliefs, values, and norms. They often base their proposals for public policy on appeals to the “common good” or “public welfare” or “public interest” (for example, Cahill, 1997; Haas, letter, 1997; Duff, 1997; Dorff, 1997; Sachedina, 1997).

Religious perspectives on public policies regarding human cloning vary for several reasons. One critical factor is whether the tradition views every possible act of cloning humans as intrinsically evil (as, for example, Roman Catholicism does) or whether it recognizes that cloning humans could conceivably be justified in some circumstances, however few they may be (as, for example, many in the Jewish tradition do). The Roman Catholic tradition argues that the very use of cloning techniques to create human beings is contrary to human dignity: “One may not use, even for a single instance, a means for achieving a good purpose which intrinsically is morally flawed” (Pope John Center, 1997, p. 4). And, for that tradition, creating a child through human cloning is intrinsically morally flawed. Some thinkers in other traditions also hold that such an action is always morally wrong, whatever good might come from it (see Meilaender, 1997).

By contrast, some other religious thinkers believe that cloning a human to create a child could be religiously and morally acceptable under certain conditions. They may view the technology as “morally neutral” (Dorff, 1997) and then consider which uses are morally justified; or they may “oppose human cloning from matured (differentiated) cells except in the most exceptional circumstances” and then identify those exceptional circumstances.

Two scenarios are quite common. The first one involves cloning a sterile person to create a child. Rabbi Tendler poses the case of “a young man who is sterile, whose family was wiped out in the Holocaust, and [who] is the last of a genetic line.” Rabbi Tendler says “I would certainly clone him” (Tendler, 1997, transcript, p. 35). The debate about this type of case hinges in part on different views of infertility. The Jewish tradition often views infertility as an “illness” and thus brings it under the responsibility to heal. According to others, for example, some in the Protestant tradition, the problem of infertility is not serious enough to warrant research into or actual human cloning (see Duff, 1997, p. 5).

A second case involves cloning a person who has a serious and perhaps fatal disease and needs a compatible source of biological material, such as bone marrow. Rabbi Dorff, for instance, holds that it would be “legitimate from a moral and a Jewish point of view” to clone a person with leukemia with the intent of transplanting bone marrow from the created child as long as the “parents” intend to raise the child as they would raise any other child (Dorff, 1997, pp. 4-5; see also Tendler, 1997). Some Protestants concur on this case, even when they reject the first type of case (see Duff, 1997, p. 4). Those who consider the second type of case justifiable rule out destruction or abandonment of the created child, as well as the imposition of serious risks of harm. Indeed, acceptance of either type of hypothetical case—as well as a third type of case involving the cloning of a dying child—presupposes that the procedure is safe for the child

created by cloning. Other conditions include the protection of the created child's rights and the lack of acceptable alternatives to cloning persons in such cases.

Those who view cloning humans as intrinsically wrong may also respond sympathetically and compassionately to people's suffering when they are infertile or have a disease that brings death or disability. However, they usually hold that the good of overcoming this suffering does not justify cloning humans: Cloning "is entirely unsuitable for human procreation even for exceptional circumstances" (Pope John Center, p. 4). Indeed, religious critics may view the exceptional circumstances featured in the cases as "temptations" to be resisted (see Meilaender, 1997, p. 5).

Some rough correlations hold between evaluations of particular cases and proposals for public policy. Religious thinkers who view the cloning of a human being as intrinsically wrong, i.e., wrong in and of itself, under any and all circumstances, tend to support a permanent ban on cloning humans through legislative and other means. Any use of cloning technology to create a human child abuses that technology, which is, however, acceptable in animal reproduction. By contrast, religious thinkers who hold that, in some conceivable circumstances, it could be morally justifiable to clone a person to create a child tend to support public policies that regulate the procedure, with varying restrictions, or that ban the procedure for the time being or until certain conditions are met. In assessing public policies, this second group is particularly concerned to prevent potential abuses of the technology in cloning humans rather than condemning all uses. For instance, they may hold that the government should impose some regulations on cloning "to prevent the most egregious abuses" (Dorff, letter, 1997). Some "egregious abuses," such as creating people for organ transplants and then discarding their remains, would already be prohibited by criminal law, but new laws and policies may be needed to prevent others.

Most religious thinkers who recommend public policies on cloning humans propose either a ban or restrictive regulation. A few examples will suffice. On March 6, 1997, the Christian Life Commission of the Southern Baptist Convention issued a resolution entitled "Against Human Cloning," which supported President Clinton's decision to prohibit federal funding for human-cloning research and requested "that the Congress of the United States make human cloning unlawful." The resolution also called on "all nations of the world to make efforts to prevent the cloning of any human being."

The Vatican's 1987 Instruction on Respect for Human Life (Donum Vitae) argued for a legal prohibition of human cloning, as well as many other reproductive technologies. Official Roman Catholic statements since that time have condemned non-therapeutic research on human embryos and human cloning and have called on governments around the world to enact prohibitive legislation. Most recently, in the wake of the cloning of "Dolly," a Vatican statement reiterated the basic teaching of Donum Vitae: "A person has the right to be born in a human way. It is to be strongly hoped that states ... will immediately pass a law that bans the application of cloning of humans and that in the face of pressures, they have the force to make no concessions"

1 ("Vatican Calls for Ban," 1997).

2 By contrast, Rabbi Elliot Dorff argues that "human cloning should be regulated, not
3 banned." He holds that "the Jewish demand that we do our best to provide healing makes it
4 important that we take advantage of the promise of cloning to aid us in finding cures for a variety
5 of diseases and in overcoming infertility." However, "the dangers of cloning . . . require that it be
6 supervised and restricted." More specifically, "cloning should be allowed only for medical
7 research or therapy; the full and equal status of clones with other fetuses or human beings must
8 be recognized, with the equivalent protections guarded; and careful policies must be devised to
9 determine how cloning mistakes will be identified and handled" (Dorff, 1997). Although Dorff
10 stresses legislation, particularly to regulate privately funded research, he recognizes that
11 legislation will be only partially effective, and for that reason calls for increased attention to
12 hospital ethics committees and institutional review boards, in part because of the self-regulation
13 involved. Hence, although legislation is important "to ban the most egregious practices," most
14 supervision "should come from self-regulation akin to what we already have in place for
15 experiments on human subjects"(Dorff, 1997, p. 15). Many religious thinkers also stress public
16 and professional education.

17 Several factors other than moral judgments about the moral acceptability or
18 unacceptability of particular cases enter into proposals for public policy. They include, along
19 with the various religious-moral arguments—for example, about the family—already examined
20 in this chapter, the history of eugenics, particularly the Nazi experience; fear of "man's mastery
21 over man" (Tendler, 1997); the risk of social discrimination and coercion; and the risks of
22 psychological harm to the child created by cloning a human. The most fundamental concern,
23 which is addressed more fully in the Chapter Four, focuses on unknown physical risks to the
24 child (see, for example, Tendler, 1997, p. 3; testimony). Many supporters of a ban or regulation
25 also want to ensure that it will be narrowly and tightly drawn in order to permit necessary and
26 potentially beneficial research.

27 One important background policy issue for some religious thinkers concerns justice,
28 fairness, or equity in the allocation of resources. Public decisions about funding research, such as
29 research on cloning humans, involve more than assessments of safety and the broad ethical
30 questions that have already been raised in this chapter and will be examined more fully in the
31 next chapter. They also involve setting priorities in the allocation of funds (see Sachedina, letter,
32 1997). Hence, one Protestant theological ethicist argues that society should not proceed with
33 research into cloning humans until it considers the larger questions of allocation, including the
34 "responsible use of limited resources" (Duff, 1997, pp. 9). One standard of evaluation that
35 focuses on the common good targets (a) the most serious questions of health and disability, and
36 (b) the welfare of society's most vulnerable members (Duff, 1997, p. 9).

37 Conclusions

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1 The wide variety of religious traditions and beliefs epitomizes the pluralism of American
2 culture. Moreover, religious perspectives on cloning humans differ in fundamental premises,
3 modes of reasoning, and conclusions. As a result, there is no single "religious" view on cloning
4 humans, any more than for most moral issues in biomedicine. Nevertheless, discourse on many
5 contested issues in biomedicine still proceeds across religious traditions, as well as secular
6 traditions. Specifically with regard to cloning humans to create children, some religious thinkers
7 believe that this technology could have some legitimate uses and thus could be justified under
8 some circumstances if perfected; however, they may argue for regulation because of the danger
9 of abuses or even for a ban, perhaps temporary, in light of concerns about safety. Other religious
10 thinkers deny that this technology has any legitimate uses, contending that it always violates
11 fundamental moral norms, such as human dignity. Such thinkers often argue for a legislative ban
12 on all cloning of humans to create children. Finally, religious communities and thinkers draw on
13 ancient and diverse traditions of moral reflection to address the cloning of humans, a subject they
14 have debated off and on over the last thirty years. For some, fundamental religious beliefs and
15 norms provide a clear negative answer: It is now and will continue to be wrong to clone a human.
16 Others, however, hold that more reflection is needed, given new scientific and technological
17 developments, to determine exactly how to interpret and evaluate the prospect of human cloning
18 in light of fundamental religious convictions and norms.

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Chapter Four

ETHICAL CONSIDERATIONS

The prospect of creating children through somatic cell nuclear transfer has elicited widespread resistance. Much of this reaction can be attributed to fears about harms to the children who may result, particularly psychological harms associated with a possibly diminished sense of individuality and personal autonomy. Others express concern about a degradation in the quality of parenting and family life if children's physical development were no longer as unpredictable, especially if parents were to confuse the predictability of certain of their children's physical characteristics with the predictability of their personality and character. And virtually all people agree that the current risks of physical harm to children associated with somatic cell nuclear transplantation cloning justify a prohibition at this time on such experimentation. In addition to concerns about specific harms to children, people have frequently expressed fears that a widespread practice of such cloning would undermine important social values, such as opening the door to a form of eugenics or by tempting some to manipulate others as if they were objects instead of persons, and accepting the moral boundaries inherent in the human condition. Arrayed against these concerns are other important social values, such as protecting personal choice, maintaining privacy the freedom of scientific inquiry, and encouraging the possible development of new biomedical breakthroughs. As somatic cell nuclear transfer cloning could represent a means of human reproduction for some people, limitations on that choice must be made only when the societal benefits of prohibition clearly outweigh the value of maintaining the private nature of such highly personal decisions. Especially in light of some arguably compelling cases for attempting to create a child through somatic cell nuclear transfer, the ethics of policymaking must strike a balance between the values we, as a society, wish to reflect and the freedom of individual choice and any liberties we propose to limit.

* * * * *

One of the key challenges for the Commission has been to understand many of the moral and religious objections to cloning human beings using somatic cell nuclear transfer as well as to investigate and articulate the widespread intuitive disapproval of cloning human beings in this manner. This challenge included an initial attempt to examine the plausibility and persuasion of these objections. These concerns then had to be tested against both those philosophical responses that are more positive regarding such cloning as well as against certain arguably compelling and specific cases for deploying this technology. In short, NBAC has sought to understand and, in some cases, to clarify the diversity of reactions to this new technology.¹

¹In support of its analysis, NBAC commissioned a paper written by Dan Brock, Brown University, titled "Cloning Human Beings: An Assessment of the Ethical Issues Pro and Con." Some of the material in this chapter is derived from that paper.

Here are
 - Ethical concerns about degradation in parenting and family life if parents seek excessive control over children's traits. (↓ tolerance)
 as well
 would be attempted to

1 Religious perspectives were presented in the previous chapter. This chapter focuses on ethical
2 principles not tied to any particular religious tradition, although these broad principles may be
3 incorporated in the teachings of many religions.

4 The task is made quite difficult by the fact that neither moral philosophers nor religious
5 thinkers can agree on the "best" moral theory; indeed, they often cannot even agree on the
6 practical implications of any single theory. For example, some people base their arguments on an
7 assessment of the particular harms and benefits that would flow to individuals and to society if
8 somatic cell nuclear transfer techniques were to become commonplace. Others express their
9 views by arguing about overarching rights—the child's right to individuality and dignity versus
10 the nucleus donor's right to procreate or the scientist's right to do research. And while moral and
11 even human rights are not necessarily understood as absolute, a choice to violate such rights
12 requires more than a simple balancing of benefits over harms.

13 While some of the risks and benefits of somatic cell nuclear cloning of human beings are
14 well enough understood to support the conclusion that it should not be permitted at this time, the
15 difficult task of striking the balance among competing rights and interests needs more time for
16 discussion and development. This chapter reviews some of these arguments which may serve as
17 the starting point for a profound and sustained reflection on the significance of creating children
18 through somatic cell nuclear transfer.

19 The following discussion of issues raised by such cloning begins with an important
20 caveat. Any research or clinical experiment on creating a child in this manner would involve the
21 creation of an embryo. That is, the fusion of a human somatic cell and an egg whose nucleus has
22 been removed would produce a human embryo, with the apparent potential to be implanted *in*
23 *utero* and developed to term. Ethical concerns surrounding the issues of embryo research, absent
24 the implantation and carrying to term of an embryo, have recently received extensive analysis and
25 deliberation in our country (National Institutes of Health, 1994). Indeed, as described in Chapter
26 Five, federal funding for human embryo research is severely restricted, although there are few
27 restrictions on human embryo research carried out in the private sector using non-federal funds.
28 NBAC did not revisit this issue in the context of this report.

29 **Potential for Physical Harms**

30 There is one basis of opposition to somatic cell nuclear transfer cloning on which almost
31 everyone can agree. For reasons outlined in Chapter Two, there is virtually universal concern
32 regarding the current safety of attempting to use this technique in human beings. Even if there
33 were a compelling case in favor of creating a child in this manner it would have to yield to one
34 fundamental principle of both medical ethics and political philosophy—the injunction, as it is
35 stated in the Hippocratic canon, to “first do no harm.” In addition, the avoidance of physical and
36 psychological harm was established as a standard for research in the Nuremberg Code, 1946-49.
37 At this time, the significant risks to the fetus and physical well being of a child created by

1 somatic cell nuclear transplantation cloning outweigh arguably beneficial uses of the technique.

2 It is important to recognize that the technique that produced Dolly the sheep was
3 successful in only 1 of 277 attempts. If attempted in humans, it would pose the risk of hormonal
4 manipulation in the egg donor; multiple miscarriages in the birth mother; and possibly severe
5 developmental abnormalities in any resulting child. Clearly the burden of proof to justify such an
6 experimental and potentially dangerous technique falls on those who would carry out the
7 experiment. Standard practice in biomedical science and clinical care would never allow the use
8 of a medical drug or device on a human being on the basis of such a preliminary study and
9 without much additional animal research. Moreover, when risks are taken with an innovative
10 therapy, the justification lies in the prospect of ~~curing an otherwise untreatable~~ illness in a ^{treating}
11 patient, whereas here no patient is at risk until the innovation is employed. Thus, no
12 conscientious physician or Institutional Review Board should approve attempts to use somatic
13 cell nuclear transfer to create a child at this time. For these reasons, prohibitions are warranted
14 on all attempts to produce children through nuclear transfer from a somatic cell at this time.

15 Even on this point, however, NBAC has noted some difference of opinion. Some argue,
16 for example, that prospective parents are already allowed to conceive, or to carry a conception to
17 term, when there is a significant risk—or even certainty—that the child will suffer from a serious
18 genetic disease. Even when others think such conduct is morally wrong, the parents' right to
19 reproductive freedom takes precedence. Since many of the risks believed to be associated with
20 somatic cell nuclear transfer may be no greater than those associated with genetic disorders, some
21 contend that such cloning should be subject to no more restriction than other forms of
22 reproduction (Brock, 1997).

23 And, as in any new and experimental clinical procedure, harms cannot be accurately
24 determined until trials are conducted in humans. Law professor John Robertson noted before
25 NBAC on March 13, 1997 that:

26 “[The] first transfer [into a uterus] of a human [embryo] clone [will occur] before
27 we know whether it will succeed. . . [Some have argued therefore] that the first
28 transfers are somehow unethical. . . experimentation on the resulting child, because
29 one does not know what is going to happen, and one is. . . possibly leading to a
30 child who could be disabled and have developmental difficulties. . . [But the] child
31 who would result would not have existed but for the procedure at issue, and [if]
32 the intent there is actually to benefit that child by bringing it into being. . . [this]
33 should be classified as experimentation for [the child's] benefit and thus it would
34 fall within recognized exceptions. . . We have a very different set of rules for
35 experimentation intended to benefit [the experimental subject]”(Robertson, 1997).

36 But the argument that somatic cell nuclear transfer cloning experiments are “beneficial”
37 to the resulting child rest on the notion that it is a “benefit” to be brought into the world as

1 compared to being left unconceived and unborn. This metaphysical argument, in which one is
2 forced to compare existence with non-existence, is problematic. Not only does it require us to
3 compare something unknowable—non-existence—with something else, it also can lead to absurd
4 conclusions if taken to its logical extreme. For example, it would support the argument that there
5 is no degree of pain and suffering that cannot be inflicted on a child, provided that the alternative
6 is to never have been conceived. Even the originator of this line of analysis rejects this
7 conclusions.²

8 In addition, it is true that the actual risks of physical harm to the child born through
9 somatic cell nuclear transfer cannot be known with certainty unless and until research is
10 conducted on human beings. It is likewise true that if we insisted on absolute guarantees of no
11 risk before we permitted any new medical intervention to be attempted in humans, this would
12 severely hamper if not halt completely the introduction of new therapeutic interventions,
13 including new methods of responding to infertility. The assertion that we should regard attempts
14 at human cloning as “experimentation for [the child’s] benefit” is not persuasive.

15 Cloning and Individuality

16 In addition to physical harms, many worry about psychological harms associated with
17 such cloning. One of the forms of psychological harm most frequently mentioned is the possible
18 loss of a sense of uniqueness.

19 Many argue that somatic cell nuclear transfer cloning creates serious issues of identity
20 and individuality and forces us to reconsider how we define ourselves. In his testimony before
21 NBAC March 13, 1997, Gilbert Meilaender commented on the importance of genetic uniqueness
22 not only for individuals but in the eyes of their parents:

23 “Our children begin with a kind of genetic independence of us, their parents.
24 They replicate neither their father nor their mother. That is a reminder of the
25 independence that we must eventually grant to them and for which it is our duty to
26 prepare them. To lose even in principle this sense of the child as gift will not be

²There is one argument that has been used by several commentators to undermine the apparent
significance of potential harms to a child created through somatic cell nuclear transfer (Chadwick 1982;
Robertson 1994, 1997; Macklin 1994). The point derives from a general problem, called the non-identity
problem, posed by the philosopher Derek Parfit and not originally directed to human cloning (Parfit 1984).
This view argues that all the psychological burdens and pressures of having been born via such cloning are
not net harms to the resulting child because they are not worse than no life at all. Parfit does not accept the
above argument as sound. Instead, he believes that if one could have a different child without these
psychological burdens (for example, by using a different method of reproduction) there is as strong a moral
reason to do so (Brock 1995).

*and
1995*

good for children”(Meilaender, 1997).

The concept of creating a genetic twin, although separated in time, is one aspect of somatic cell nuclear transfer cloning that most find both troubling and fascinating. The phenomenon of identical twins has intrigued human cultures across the globe, and throughout history (Schwartz, 1996). It is easy to understand why identical twins hold such fascination. Common experience demonstrates how distinctly different twins are, both in personality and in personhood. At the same time, observers cannot help but imbue identical bodies with some expectation that identical persons occupy those bodies, since body and personality remain intertwined in human intuition. With the prospect of somatic cell nuclear transfer cloning comes a scientifically inaccurate but nonetheless instinctive fear of multitudes of identical bodies, each housing personalities that are somehow less than distinct, less unique, and less autonomous than usual.

Is there a moral or human right to a unique identity, and if so would it be violated by this manner of human cloning? For such somatic cell nuclear transfer cloning to violate a right to a unique identity, the relevant sense of identity would have to be genetic identity, that is a right to a unique unrepeatable genome. Even with the same genes, two individuals—for example homozygous twins—are distinct and not identical, so what is intended must be the various properties and characteristics that make each individual qualitatively unique and different than others. Does having the same genome as another person undermine that unique qualitative identity?

Along these lines of inquiry some question whether reproduction using somatic cell nuclear transfer would violate what philosopher Hans Jonas called a right to ignorance, or what philosopher Joel Feinberg called a right to an open future (Jonas 1974; Feinberg 1980). Jonas argued that human cloning, in which there is a substantial time gap between the beginning of the lives of the earlier and later twin, is fundamentally different from the simultaneous beginning of the lives of homozygous twins that occur in nature. Although contemporaneous twins begin their lives with the same genetic inheritance, they also begin their lives or biographies at the same time, in ignorance of what the twin who shares the same genome will by his or her choices make of his or her life. To whatever extent one's genome determines one's future, each life begins ignorant of what that determination will be, and so remains as free to choose a future as are individuals who do not have a twin. In this line of reasoning, ignorance of the effect of one's genome on one's future is necessary for the spontaneous, free, and authentic construction of a life and self.

A later twin created by cloning, Jonas argues, knows, or at least believes he or she knows, too much about him or herself. For there is already in the world another person, one's earlier twin, who from the same genetic starting point has made the life choices that are still in the later twin's future. It will seem that one's life has already been lived and played out by another, that one's fate is already determined, and so the later twin will lose the spontaneity of authentically

1 creating and becoming his or her own self. One will lose the sense of human possibility in freely
2 creating one's own future. It is tyrannical, Jonas claims, for the earlier twin to try to determine
3 another's fate in this way.

4 And even if it is a mistake to believe such crude genetic determinism according to which
5 one's genes determine one's fate, what is important for one's experience of freedom and ability to
6 create a life for oneself is whether one thinks one's future is open and undetermined, and so still
7 to be largely determined by one's own choices. One might try to interpret Jonas' objection so as
8 not to assume either genetic determinism, or a belief in it. A later twin might grant that he or she
9 is not destined to follow in his or her earlier twin's footsteps, but that nevertheless the earlier
10 twin's life would always haunt the later twin, standing as an undue influence on the latter's life,
11 and shaping it in ways to which others' lives are not vulnerable.

12 In a different context, and without applying it to human cloning, Feinberg has argued for
13 a child's right to an open future. This requires that others raising a child not close off the future
14 possibilities that the child would otherwise have by constructing his or her own life. One way
15 this right to an open future would be violated is to deny even a basic education to a child, and
16 another way might be to create it as a later twin so that it will believe its future has already been
17 set for it by the choices made and the life lived by its earlier twin.

18 On the other hand, all of these concerns are not only quite speculative, but are directly
19 related to certain specific cultural values. Someone created through the use of somatic cell
20 nuclear transfer techniques may or may not believe that their future is relatively constrained.
21 Indeed, they may believe the opposite. In addition, quite normal parenting usually involves many
22 constraints on a child's behavior that children may resent. Moreover, Feinberg's argument does
23 not apply, if the belief is false and it can be shown to be false.

24 Finally, there is an irony to some of these concerns, as pointed out by Robertson.

25 "[O]pponents talk about the importance of having a unique genome and how
26 cloning might rob a child of a unique identity. At the same time, however, they
27 want to deny the importance of genes alone in creating identity, so there is a kind
28 of tension there in their comments" (Robertson, 1997).

29 Thus, a central difficulty in evaluating the implications for somatic cell nuclear transfer
30 cloning of a right either to ignorance or to an open future, is whether the right is violated merely
31 because the later twin may be likely to believe that its future is already determined, even if that
32 belief is clearly false and supported only by the crudest genetic determinism. Moreover, what
33 such a twin is likely to believe will depend on the facts that emerge and what scientists and
34 ethicists claim.

Cloning, Values, and the Family

Among those concerns that are not focused on arguments about harm to the child are a set of worries about use of such cloning as a means of control. There are concerns, for example, about possibly generating large numbers of people whose life choices are limited by their own constrained self-image or by the constraining expectations of others. From this image of less-than-autonomous children comes the fear, however misplaced, of technology creating armies of cloned soldiers, each diminished in his or her physical individuality and thereby diminished in their psychological autonomy. Similarly, this expectation of diminished autonomy underlies the eugenic arguments that have led many to speculate about the possibility of cloning "desirable" or "evil" people, ranging from actors to dictators of various stripes to distinguished religious leaders. Complicating matters even further, this misplaced belief in the ability of genes to fully determine behavior and personality amplifies the image, so that in the end one imagines being able to make either armies of complacent workers, crazed soldiers, brilliant musicians, or beatific saints.

Although such fears are based, as noted in Chapter Two, on gross misunderstandings of human biology and psychology, they are nonetheless fears that have been voiced. In addition, these same concerns also manifest themselves in fears that underlie the characterization of somatic cell nuclear transfer cloning as a form of "making" children rather than "begetting" children. With cloning, the total genetic blueprint of the cloned individual is selected and determined by the human artisans. This, according to Kass,

"...would be taking a major step into making man himself simply another one of the man made things. Human nature becomes merely the last part of nature to succumb to the technological project which turns all of nature into raw material at human disposal. . .As with any product of our making, no matter how excellent, the artificer stands above it, not as an equal but as a superior, transcending it by his will and creative prowess" (Kass, 1997).

For many, this kind of relationship is inconsistent with an ideal of parenting, in which parents embrace not only the similarities between themselves and their children but also the differences, and in which they accept not only the developments they sought to bring about through care and teaching but also the serendipitous developments they never planned for or anticipated (Rothenberg, 1997).

Of course, parents already exercise great control over their offspring, through means as varied as contraception to control of the timing and spacing of births, to genetic screening and use of donor gametes to avoid genetic disorders, to organized medical and educational interventions to guide physical and intellectual development. These interventions exist along a spectrum of control over development. Somatic cell nuclear transfer cloning, some fear, offers the possibility of virtually complete control over one important aspect of a child's development,

his or her genome, and it is the completeness of this control, even if only over this partial aspect of human development, that is alarming to many people and invokes images of manufacturing children according to specification. The lack of acceptance this implies for children who fail to develop according to expectations, and the dominance it introduces into the parent-child relationship, is viewed by many as fundamentally at odds with the acceptance, ~~indeterminacy,~~ ^{and} ~~and unconditional love that is currently associated with parenting.~~ ^{openness} Meilaender addressed both ^{and} the mystery of reproduction and fears about it veering toward a means of production in his testimony before NBAC. ^{unconditional love}

^{Characteristic of good}
 "But whatever we say of [other reproductive technologies], surely human cloning would be a new and decisive turn on this road. Far more emphatically a kind of production. Far less a surrender to the mystery of the genetic lottery which is the mystery of the child who replicates neither Father nor Mother but incarnates their union. Far more an understanding of the child as a product of human will" (Meilaender, 1997).

Questions are raised, as well, about the effect such interventions will have on a particular child. Will the child himself or herself feel less independent from the nucleus donor than a child ordinarily would from a parent? Will the knowledge of how one's genetic profile developed in another person at another time leave the child feeling that his character is as predetermined as his eye or hair color? Even if the child feels completely independent of the nucleus donor, will others regard the child as a copy or a successor to that donor? If so, will such expectations on the part of others begin to affect the child's self image?

^{warp the child's emerging self-understanding.}

Finally, some critics of such cloning are concerned that the legal or social status of the child arising from nuclear transfer of somatic cells may be uncertain. For some, the disparity between the child's genetic and social identity threatens the stability of the family. Is the child who results from somatic cell nuclear transfer the sibling or the child of its parents? The child or the grandchild of its grandparents? From this perspective the child's psychological and social well-being may be in doubt or even endangered. Ambiguity over parental roles may undermine the child's sense of identity. It may be harder for a child to achieve independence from a parent who is also his or her twin.

At the same time, others are not persuaded by such objections. Children born through assisted reproductive technologies may also have complicated relationships to genetic, gestational, and rearing parents. Skeptics of this point of view note that there is no evidence that confusion over family roles has harmed children born through assisted reproductive technologies, although the subject has not been carefully studied.

Potential Harms to Important Social Values

Those with grave reservations about somatic cell nuclear transfer cloning ask us to

1 imagine a world in which cloning human beings via somatic cell nuclear transfer were permitted
2 and widely practiced. What kind of people, parents, and children would we become in such a
3 world? Opponents fear that such cloning to create children may disrupt the interconnected web
4 of social values, practices, and institutions that support the healthy growth of children. The use of
5 such cloning techniques might encourage the undesirable attitude that children are to be valued
6 according to how closely they meet parental expectations, rather than loved for their own sake.
7 In this way of looking at families and parenting, certain values are at the heart of those
8 relationships, values such as love, nurturing, loyalty, and steadfastness. In contrast, a world in
9 which such cloning were widely practiced would give, the critics claim, implicit approval to
10 vanity, narcissism, and avarice. To these critics, changes that undermine those deeply prized
11 values should be avoided if possible. At a minimum, such undesirable changes should not be
12 fostered by public policies.

13 On the other hand, others are not persuaded by these objections. First, many social
14 observers point out that if strongly held moral values are in decline, there are likely many
15 complex reasons for this, which would not be addressed by a ban on cloning in this fashion.
16 Furthermore, skeptics argue that people can, and do, adapt in socially redeeming ways, to new
17 technologies. In their view, a child born through somatic cell nuclear transfer could be loved and
18 accepted like any other child, and not disrupt important family and kinship relations.

19 The strength of public reaction, however, reflects a deep concern that somehow many
20 important social values could be harmed in a society where such cloning were widely used. In
21 his testimony before the Commission on March 13, 1997, bioethicist Leon Kass summarized
22 many of the widely held concerns regarding the possibility of cloning human beings via somatic
23 cell nuclear transfer when he noted,

24 "Almost no one sees any compelling reason for human cloning. Almost everyone
25 anticipates its possible misuses and abuses. Many feel oppressed by the sense that
26 there is nothing we can do to prevent it from happening and this makes the
27 prospect seem all the more revolting. Revulsion is surely not an argument....But
28 ... in crucial cases repugnance is often the emotional bearer of deep wisdom
29 beyond reason's power fully to articulate it" (Kass, 1997).

30 But some people, however, argue against relying on moral intuition to set public policy.
31 While it is certainly true that repugnance may be the bearer of wisdom, it may also be the bearer
32 of simple and thoughtless prejudice. In her testimony before NBAC on March 14, 1997,
33 bioethicist Ruth Macklin challenged the inclination to take as axiomatic the proposition that to be
34 born as a result of using these techniques is to be harmed or at least to be wronged.

35 "Intuition has never been a reliable epistemological method, especially since
36 people notoriously disagree in their moral intuitions. . . If objectors to cloning can
37 identify no greater harm than a supposed affront to the dignity of the human

species, that is a flimsy basis on which to erect barriers to scientific research and its applications" (Macklin, 1997).

Nevertheless, opponents assert that this new type of cloning tempts human beings to transgress moral boundaries and to grasp for powers that are properly outside human control. Ancient Greek literature and many Biblical interpretations emphasize that human beings occupy a moral position between other forms of life and the divine. In particular, humans should not consider themselves as omnipotent over nature. From this perspective, respecting limits is to respect the appropriate place of humankind in the universe and to ensure that technology is not allowed to push aside critical social and moral commitments. This view need not be tied to a single religious doctrine, a particular view of God, or even a belief in God. However, these objections are often expressed in religious terms. For example, critics talk of how the ability to create children through somatic cell nuclear transfer may tempt us to seek immortality, to usurp the role of God, or to violate divine commands.

On the other hand, some observers do not see this type of cloning as dramatically new or extreme, especially when compared to other assisted reproductive technologies. Robertson notes

"In an important sense cloning is not the most radical thing on the horizon. Much more significant, I think, would be the ability to actually alter or manipulate the genome of offspring. Cloning takes a genome as it is. . . and might replicate it . . . [T]hat is much less ominous than having an ability to take a given genome and either add or take out a gene which could then lead to a child being born with characteristics other than it would have had with the genome it started with" (Robertson, 1997).

Finally, critics have also raised questions about an inappropriate use of scarce resources. The generation of children through somatic cell nuclear transfer would divert scarce resources, including the skills of researchers and clinicians, from more pressing social and medical needs. These considerations about allocation of resources are particularly pertinent if public funds would be involved. In the words of theologian Nancy Duff:

"When considering research into human cloning we must look at the responsible use of limited resources. . . [I]t is mandatory to ask whether other research projects will serve a greater number of people than research on human cloning and take the answer to that seriously" (Duff, testimony, 1997).

[Human Dignity]
Commodification, Objectification, and the Good Life

Treating Persons as Objects

The philosopher Martha Nussbaum has argued that the goal of political organizations is to provide people with "the conditions in which a good human life can be chosen and lived, not simply at the allotment of commodities, but at making people able to function in certain human

ways" (Nussbaum, 1988). To do this, it is important to identify the essential qualities of humanity that must be nurtured in order to permit the good life to flourish (Nussbaum, 1990). Her list of "basic human functional categories" includes, the quality of "separateness," or "being able to live one's own life and nobody else's; being able to live one's own life in one's very own surroundings and context."

Separateness is particularly pertinent to somatic cell nuclear transfer cloning. One of the concerns raised by opponents focuses on whether the ability to completely determine a child's genetic make-up will have the effect of lessening the child's sense of separateness and autonomy, thereby turning the child into an "object" rather than a "person." This concern acts as an often unspoken assumption underlying discussions of whether such cloning amounts to "making" rather than "begetting" children; whether prior knowledge of how one's genetic make-up expressed itself in an older twin will serve to constrain one's imagination about what the future can hold or how it can be shaped to one's desires; and whether the child who is created in this manner will be viewed as less than fully separate and equal to the older twin whose nucleus was used. In sum, will being cloned from the somatic cell of an adult make the child less of a "person" whose humanity is to be nurtured toward attainment of the good life?

One reason this discussion can be hard to capture and to articulate is that certain terms, such as "person," are used differently by different people.³ What is common to these various views, however, is a shared understanding that being a "person" is different from being the manipulated "object" of other people's desires and expectations. Writes legal scholar Margaret Radin,

"The person is a subject, a moral agent, autonomous and self-governing. An object is a non-person, not treated as a self-governing moral agent . . . [By]

³ Moral philosophers think about personhood when they construct and deploy their views of human choice and moral agency. For Kantians, personhood is about free will and reason. From the point of view of Kantian moral personality, all of us are identical as persons. Philosophers of mind think about personhood when they try to figure out what constitutes personal identity. For many of these philosophers, personal identity means having a continuous life story that incorporates a past and a future for oneself. From the point of view of personal identity, all of us are different, unique, as persons. Psychoanalysts think about personhood when they relate the constants of human life and development to broad personality structures. From the psychoanalytic point of view, each of us manifests the same dynamic personality structures, yet no two of us do so in exactly the same way; we are all the same and also all different. Welfare rights activists and human rights activists may think about personhood: what is the minimum of necessary resources for a fully human life? Some medical ethicists think about personhood while trying to decide at what point does life cease to be a human life worth living? Political theorists at times think about personhood in the context of trying to understand what are the basics of individuality that the state should recognize or underwrite? Parents think about personhood: what part do I play in making possible the fullest kind of human-ness for my children?"

1 'objectification of persons,' we mean, roughly, "what Kant would not want us to
2 do."⁴

3 [That is, to objectify a person is to ~~subject the person to manipulation~~ ^{or well-being excessively} without regard to the
4 person's own desires, to control the person, and to ~~treat the person as one would things that can~~ ^{act toward the person}
5 be bought and sold in the marketplace.] ^{as the extremes} rather than to engage them in
a mutually-respectful relationship.

6 To those who view the intentional choice by another of one's genetic make-up as a form
7 of manipulation by others, there is a risk that somatic cell nuclear transfer cloning represents a
8 form of objectification or commodification of the child. Of course, this is precisely what genetic
9 screening and, in the future, genetic therapy, aim to do. But in those cases, the goal is to benefit
10 the child so that the child may be free of a specific disease. When such cloning is undertaken not
11 for any purported benefit of the child himself or herself, but rather to satisfy the vanity of the
12 nucleus donor, or even to serve the need of someone else, such as a dying child in need of a bone
13 marrow donor, then some would argue that it goes yet another step toward diminishing the
14 personhood of the child created in this fashion. The final insult, opponents argue, would come if
15 the child created through somatic cell nuclear transfer is regarded as somehow less than fully
16 equal to the other human beings, due to his or her diminished physical uniqueness and the
17 diminished mystery surrounding some aspects of his or her future, physical development.

18 Eugenic Concerns

19 The desire to improve on nature is as old as humankind. It has been played out in
20 agriculture through the breeding of special strains of domesticated animals and plants. With the
21 development of the field of genetics over the past 100 years came the hope that the selection of
22 advantageous inherited characteristics—called eugenics, from the Greek eugenes meaning
23 wellborn or noble in heredity—could be as beneficial to humankind as selective breeding in
24 agriculture.

25 The transfer of directed breeding practices from plants and animals to human beings is
26 inherently problematic, however. To begin, eugenic proposals require that several dubious and
27 offensive assumptions be made. First, that most, if not all people would mold their reproductive
28 behavior to the eugenic plan; in a country that values reproductive freedom, this outcome would

⁴ "Kantian ethical thought," writes Radin, "distinguishes morally between persons and objects. Rational beings possessing free will (persons) are autonomous; the moral law requires that persons be treated as ends, not means. Objects in the natural world that are not rational beings possessing free will are not persons, and may appropriately be used as means by persons. Kant's view requires that persons, moral agents, not be treated as objects, manipulated at the will of persons. Kant presented his basic principles of ethics in *Immanuel Kant, Groundwork of The Metaphysics of Morals* (1785), translated by H. J. Paton in *The Moral Law* (1948)." [Margaret Radin, "Reflections on Objectification," 65 *Southern California Law Review* 341 (November 1991), at footnote 4]

Ⓟ Some would say no more dangerous than genetic screening or, in the future, gene therapy... both control genes... but to the extent used to benefit the child, no objectification takes place.

1 be unlikely absent compulsion. Second, that means exist for deciding which human traits and
2 characteristics would be favored, an enterprise that rests on notions of selective human
3 superiority that have long been linked with racist ideology.

4 Equally important, the whole enterprise of "improving" humankind by eugenic programs
5 oversimplifies the role of genes in determining human traits and characteristics. Little is known
6 about correlation between genes and the sorts of complex, behavioral characteristics that are
7 associated with successful and rewarding human lives; moreover, what little is known indicates
8 that most such characteristics result from complicated interactions among a number of genes and
9 the environment. While cows can be bred to produce more milk and sheep to have softer fleece,
10 the idea of breeding humans to be superior would belong in the realm of science fiction even if
11 one could conceive how to establish the metric of superiority, something that turns not only on
12 the values and prejudices of those who construct the metric but also on the sort of a world they
13 predict these specially bred persons would face.

14 Nonetheless, at the beginning of this century eugenic ideas were championed by scientific
15 and political leaders and were very popular with the American public. It was not until they were
16 practiced in such a grotesque fashion in Nazi Germany that their danger became apparent.
17 Despite this sordid history and the very real limitations in what genetic selection could be
18 expected to yield, the lure of "improvement" remains very real in the minds of some people. In
19 some ways, creating people through somatic cell nuclear transfer offers eugenicists a much more
20 powerful tool than any before. In selective breeding programs, such as the "germinal choice"
21 method urged by the geneticist H.J. Muller a generation ago (Keveles, 1995), the outcome
22 depended on the usual "genetic lottery" that occurs each time a sperm fertilizes an egg, fusing
23 their individual genetic heritages into a new individual. Cloning, by contrast, would allow the
24 selection of a desired genetic prototype which would be replicated in each of the "offspring," at
25 least on the level of the genetic material in the cell nucleus.

26 It might be enough to object to the institution of a program of human eugenic
27 cloning—even a voluntary program—that it would rest on false scientific premises and hence be
28 wasteful and misguided. But that argument might not be sufficient to deter those people who
29 want to push the genetic traits of a population in a particular direction. While acknowledging
30 that a particular set of genes can be expressed in variety of ways and therefore that cloning (or
31 any other form of eugenic selection) does not guarantee a particular phenotypic manifestation of
32 the genes, they might still argue that certain genes provide a better starting point for the next
33 generation than other genes.

34 The answer to any who would propose to exploit the science of cloning in this way is that
35 the moral problems with a program of human eugenics go far beyond practical objections of
36 infeasibility. Some objections are those that have already been discussed in connection with the
37 possible desire of individuals to use somatic cell nuclear transfer that the creation of a child
38 under such circumstances could result in the child being objectified, could seriously undermine

1 the value that ought to attach to each individual as an end in themselves, and could foster
2 inappropriate efforts to control the course of the child's life according to expectations based on
3 the life of the person who was cloned.

4 In addition to such objections are those that arise specifically because what is at issue in
5 eugenics is more than just an individual act, it is a collective program. Individual acts may be
6 undertaken for singular and often unknown or even unknowable reasons, whereas a eugenics
7 program would propagate dogma about the sorts of people who are desirable and those who are
8 dispensable. That is a path that humanity has tread before, to its everlasting shame. And it is a
9 path to whose return the science of cloning should never be allowed to give even the slightest
10 support.

11 **Arguments for Maintaining Personal Autonomy and Freedom of Inquiry**

12 Arrayed against these concerns about the societal effects of cloning human beings via
13 somatic cell nuclear transfer are arguments for maintaining individual choice over whether to use
14 the technology. These arguments are made on five separate grounds: first, that there is a general
15 presumption in favor of individual liberty; second, that certain actions, such as human
16 reproduction, are particularly personal and should remain free of constraint; third, as a society we
17 ought not limit the freedom of scientific inquiry; fourth, that there are some reasons to create a
18 child through somatic cell nuclear transfer so compelling they should transcend objections to the
19 practice even if it should otherwise be prohibited; and finally, that many of the objections to the
20 use of this technique are largely speculative and unproven.

21 **Presumptions in Favor of Personal Autonomy**

22 The presumption in favor of individual liberty stems from a consensus within the United
23 States that one of the most important values we share is a commitment to personal autonomy. In
24 part, this commitment is maintained because of the widespread fear that one's own personal
25 choices might be constrained if subject to collective decision making. To the extent that making
26 a personal choice is a form of personal satisfaction, then the means to maximize our collective
27 satisfaction is to make as many personal choices available as possible (Posner, 1992). In
28 addition, personal autonomy is considered valuable in and of itself, since it is viewed by many as
29 the deepest expression of one's individuality and personality, i.e., the deepest expression of one's
30 self. Thus, commentators have argued that a commitment to individual liberty requires that
31 individuals be left free to create children using somatic cell nuclear transfer if they so choose and
32 if their doing so does not cause significant harms to others (Robertson 1997; Macklin 1997).

33 But such liberty is too broad in scope to be an uncontroversial moral right (Mill 1859;
34 Rhodes 1995). As many others have pointed out, granting such untethered primacy to autonomy
35 can ignore the possibility of competing values that are held as dear in some or all circumstances.
36 Thus, principles of equality, virtue, and benevolence may compete for primacy with the principle

1 of autonomy. In her March 13, 1997 testimony before NBAC, theologian Lisa Cahill asserted
2 that

3 " . . . a excessive focus on [autonomy] can prevent us from seeing why other values
4 as well are socially important and protectable and why certain freely chosen
5 practices can still be wrong even if they do not result in immediate or quantifiable
6 harm or direct infringement on the options of other free agents. . . A narrow focus
7 on autonomy to freely choose personally preferred goals undermines our ability to
8 talk together about what would go to make up a good society and what we can do
9 concretely to move towards one."

10 Indeed, some analysts, such as legal scholar Mary Ann Glendon (1991) and sociologist
11 Amitai Etzioni (1990) have argued that the rhetoric of rights and personal autonomy has
12 obscured the correlative values of responsibility, duty, and restraint. And, indeed, while personal
13 autonomy is upheld rhetorically as an ideal, it is often also constrained on behalf of the common
14 good, even in the absence of harm to others, both in personal and public life. This still leaves
15 open, however, the question of when, in particular, other values ought to trump the value of
16 personal liberty.

17 In their book *Democracy and Disagreement* (1996) political theorists Amy Gutmann and
18 Dennis Thompson set forth some guidelines for when moral arguments ought to be allowed to
19 constrain personal liberty. Among them are: (1) a convincing argument that a particular action is
20 wrong, independent of whatever specific harms it might cause, because it violates, for example,
21 natural law, social convention, or fundamental social values; (2) that the wrong is serious enough
22 to warrant public attention and is otherwise eligible for public regulation; and (3) that regulation
23 or prohibition will not cause more harm than the action that opponents seek to prohibit.

24 ~~Constraint~~ **Reproductive Choice**

25 While the discussion of social values, above, might satisfy the first two conditions set
26 down by Gutmann and Thompson, the third condition requires more attention in this case. To
27 determine whether prohibition of somatic cell nuclear transfer cloning would cause more harm
28 than it prevents, one must examine the particular kind of choices that would be constrained.
29 Certain actions, it is argued, deserve special protection from collective decision making, and
30 human reproduction is often cited as an example. Reproduction is an intensely personal
31 phenomenon, most often commencing in the intimacy of coitus, and always resulting in the
32 creation of a parental relationship that redefines one's place in the world. Without reproduction,
33 one remains a child and perhaps a sibling. With reproduction—or with its social equivalent,
34 adoption—one becomes a parent, taking on responsibilities for another that necessarily require
35 abandoning some of the personal freedoms enjoyed before. When and how to take on such
36 responsibilities and to change one's life course is necessarily one of the most personal and
37 significant decisions imaginable.

1 It could be argued that somatic cell nuclear transfer cloning is not covered by the right to
2 reproductive freedom, because whereas assisted reproductive technologies covered by that right
3 are remedies for inabilities to reproduce sexually, somatic cell nuclear transfer cloning is an
4 entirely new means of reproduction; indeed, its critics see it as radically new and as more a
5 means of the mere "manufacturing of humans" than of reproduction. Its asexual nature, for
6 example, leads some to view it as distinctly different from reproduction, which they view as
7 inherently collaborative and sexual. This led one commentator to note that

8 "It would be possible for female lineages to proceed without any male
9 contribution at all and it would be possible for one woman to create her own child
10 using her own ovum and DNA. . . So the child who is truly the child of a single
11 parent would be a genuine revolution in human history and her or his advent
12 should be viewed with immense caution" (Cahill, 1997).

13 On the other hand, while somatic cell nuclear transfer cloning is a different means of
14 reproduction than sexual reproduction, it is nonetheless a means that can serve individuals'
15 interest in reproducing. If it is not covered by the moral right to reproductive freedom, some
16 argue, that must be not because it is a new means of reproducing, but instead because it has other
17 objectionable moral features, such as eroding human dignity or uniqueness.

18 Assuming for the sake of discussion that somatic cell nuclear transfer cloning is a form of
19 reproduction, the question remains whether reproductive freedom ought to protect its use.
20 Reproductive freedom includes not only the familiar right to choose not to reproduce, for
21 example by means of contraception, but also the right to reproduce. It is commonly understood
22 to include the use of various artificial reproductive technologies, such as *in vitro* fertilization, and
23 sperm or egg donation. But the case for permitting the use of a particular means of reproduction
24 is strongest when that means is necessary for particular individuals to be able to procreate at all.

25 It is possible that somatic cell nuclear transfer cloning could be the only technique for
26 individuals to create a genetically related child, but in other cases different means of procreating
27 would also be possible. When individuals have alternative means of procreating, cloning might
28 be chosen because it replicates a particular individual's genome. The reproductive interest in
29 question then is not simply reproduction itself, but a more specific interest in choosing what kind
30 of children to have.

31 However, the more a reproductive choice is not simply the determination of one's own
32 life but the determination of the nature of another, as in the case of cloning via somatic cell
33 nuclear transfer, the more the interests of that other person—that is the resulting child—should
34 carry moral weight in decisions that determine its nature (Annas, 1994). In addition to the
35 parents and child reproduction is also a communal phenomenon. It thrusts a new person into the
36 world, and the whole community has obligations for this new member's well being.

Thus, the decision to reproduce is rife with consequence both to the new person brought into being and to those who will live and interact with that new person. Naturally, this invites communal commentary on the wisdom of when and how this person is brought into being. And while constitutional law has viewed certain aspects of reproductive choice as fundamental rights, discourse is not so constrained. Thus, one is free to argue, as a matter of ethics, that reproductive choices ought to be made in light of communal values, even while accepting that there are administrative and political reasons for avoiding efforts to embody these moral judgements in the form of laws, whose enforcement would intrude the state into the private realm of family life and conjugal relations to an unacceptable degree.

Freedom of Scientific Inquiry

Another argument made against prohibiting efforts to attempt to create a child through somatic cell nuclear transfer focuses on the need to encourage research and scientific advances. There is no doubt that the ~~freedom of scientific inquiry~~ has been an enduring American value. Even the framers of the Constitution discussed the importance of scientific inquiry when they established a system of patents to promote scientific invention. Historically, scientific inquiry has been protected and even encouraged because of the great social import the United States places on the "sanctity of knowledge and the value of intellectual freedom."

The concept of freedom of scientific inquiry has been acknowledged by judges and legal scholars as well. For example, certain commentators argue that support for such a right to pursue knowledge could be derived from the Fourteenth Amendment right to personal liberty and the First Amendment right to free speech (Robertson, 1977; Coleman, 1996). And the U.S. Supreme Court in Branzburg v. Hayes specifically analogized the information function performed by academic researchers to that performed by the press.⁵

Other courts have similarly suggested that scholars have a "right . . . to do research and advance the state of man's knowledge."⁶ Nonetheless, other court cases specifically reject the idea that a fundamental right of scientific inquiry exists.⁷ These cases are relevant because they

⁵Branzburg v. Hayes, 408 U.S. 665, 705 (1972). Similarly, the Supreme Court stated in Meyer v. Nebraska that the right to liberty guaranteed by the Fourteenth Amendment encompassed freedom to "acquire useful knowledge . . . and generally to enjoy those privileges long recognized at common law as essential to the orderly pursuit of happiness by free men."

⁶Henley v. Wise, 303 F.Supp. 62 (N.D. Ind. 1969).

⁷Margaret S. I, 488 F.Supp. 181, 220-221 (E.D. La. 1980). See also Margaret S. v. Treen, 597 F.Supp. 636 (E.D. La. 1984), aff'd sub. nom Margaret S. v. Edwards, 794 F.2d 994 (5th Cir. 1986); Wynn v. Scott, 449 F.Supp. 1302, 1322 (N.D. Ill. 1978), aff'd sub nom., Wynn v. Carey, 599 F.2d 193 (7th Cir. 1979).

held that there is no fundamental right of medical researchers to conduct medical research on fetuses.

The importance we attach to free scientific inquiry does not mean a science without moral constraints. International statements about the ethics of research with human subjects, such as the Nuremberg Code and the Declaration of Helsinki, make it abundantly clear that science, however valuable, must observe moral boundaries. Scientific research must not endanger community safety or the rights or interests of its human subjects. Likewise, it must not inflict unnecessary suffering on animals.

^{Therefore}
~~But~~ even if scientific inquiry were found to be a protected activity, the government could regulate to protect against compelling harms, such as the current physical risks posed by somatic cell nuclear transfer techniques. The freedom to pursue knowledge is distinguishable from the right to choose the method for achieving that knowledge, since the method itself may permissibly be regulated. Although the government may not prohibit research in an attempt to prevent the development of new knowledge, it may restrict or prohibit the means used by researchers which intrude on interests in which the state has a legitimate concern (Robertson, 1977).

Thus, both the federal government and the states already regulate the researcher's methods in order to protect the rights of research subjects and community safety. Research may be restricted, for example, to protect the subject's right to autonomy and welfare by requiring informed, free and competent consent. Thus, where the government can prove that restrictions on cloning and cloning technology are sufficiently important to the general well-being of individuals or society, such restrictions are likely to be upheld as legitimate, constitutional governmental actions, even if scientists were held to have a First Amendment right of scientific inquiry (Robertson, 1977).

The Policy Maker's Dilemma: Consideration of Exceptional Cases

Even as a matter of ethics, rather than of law, it is quite possible to argue against a wholesale condemnation of somatic cell nuclear transfer cloning of human beings. Some circumstances have been identified in which the choice to create a child in this manner would be understandable, or even, as some have argued, desirable. Consider the following examples:

- A couple wishes to have children, but both adults are carriers of a lethal recessive gene. Rather than risk the one in four chance of conceiving a child who will suffer a short and painful existence, the couple considers the alternatives: to forgo rearing children; to adopt; to use donor gametes free of the recessive trait; or to use the cells of one of the adults and attempt to clone a child. Because they very much want to have some genetic link to the child they rear, ~~and because~~ they dislike the thought of introducing a third adult into their relationship in the form of a gamete donor, they opt for cloning.

to use prenatal diagnosis and selective abortion. ^{or they wish to avoid the prospect of}

- 1 • A family is in a terrible accident. The father is killed, and the only child, an infant, is
2 dying. The mother decides to use some cells from the dying infant in an attempt to use
3 somatic cell nuclear transfer to create a new child. It is the only way she can raise a child
4 who is the biological offspring of her late husband.
- 5 • The parents of a terminally ill child are told that only a bone marrow transplant can save
6 the child's life. With no other donor available, the parents attempt to clone a human
7 being from the cells of the dying child. If successful, the new child will be a perfect
8 match for bone marrow transplant, and can be used as a donor without significant risk or
9 discomfort. The net result: two healthy children, loved by their parents, who happen to be
10 identical twins of different ages.

11 In each of these examples, the impulse to attempt such cloning can be understood. In the
12 first example, the possible complications caused by having a child who is genetically identical to
13 one of the parents is weighed against the value of keeping the marital relationship free of the
14 ghost of an anonymous sperm or egg donor. In the second, the psychological complexities of
15 bearing a "replacement" child are weighed against the grief of losing not only a husband but also
16 the possibility of a child who will grow up as a physical reminder of that love. While some may
17 argue that neither case is compelling, because infertility and grief are part of human existence,
18 the intensely personal nature of that infertility or grief argues for an equally personal decision
19 about how to respond. The third case makes what is probably the strongest possible case for
20 cloning a human being, as it demonstrates how this technology could be used for lifesaving
21 purposes. Indeed, the tragedy of allowing the sick child to die because of a moral or political
22 objection to such cloning overall merely points up the difficulty of making policy in this area.

23 Some would argue that what is more important in these scenarios is how the resulting
24 child will be viewed. Macklin argues that:

25 "The ethics of these situations must be judged by the way in which the parents
26 nurture and rear the resulting child and whether they bestow the same love and
27 affection on a child brought into existence by a technique of assisted reproduction
28 as they would on a child born in the usual way" (Macklin, 1997).

29 But regardless of how one resolves the ethics of a specific situation invoking the choice to
30 create a child through somatic cell nuclear transfer, it may still be necessary to forbid the practice
31 overall, in order to protect other societal interests.

32 Moral Reasoning and Public Policies

33 "It is certainly possible that there may be no substantial benefits to society that
34 would result if human cloning were to become a reality. Yet this would constitute
35 a good argument for prohibition only if considerable harms are a likely

1 consequence. We need a realistic portrait, not a recitation of worst case science
2 fiction scenarios before we may conclude that the harms of allowing cloning to
3 proceed in a research context and even beyond are so great that even with
4 regulations and oversight consummate evil will result" (Ruth Macklin, 1997).

5 "We should proceed with research into human cloning only if compelling
6 arguments can be made for its potential benefits" (Nancy Duff, 1997).

7 Some citizens may be persuaded that the harms and wrongs described in this chapter are
8 ethically compelling and might be decisive reasons never to permit cloning via somatic cell
9 nuclear transfer. Others may be less certain about the significance of the objections, and
10 unwilling to conclude that somatic cell nuclear transfer cloning would be ethically impermissible,
11 if and when the risks could be shown to be minimal. This range of views is reflected in the
12 testimony, letters, and commissioned papers reviewed by NBAC, and is also characteristic of the
13 commissioners themselves.

14 NBAC was asked to consider whether public policy should permit, regulate, or prohibit
15 the creation of children through somatic cell nuclear transfer. The formation of public policy in
16 an area as sensitive as procreation requires careful thought and measured deliberation. In the
17 United States, governmental policies that prohibit or regulate human actions require justification
18 because of a general presumption against governmental interference in individual activities. This
19 presumption can be rebutted under various circumstances for a variety of reasons. Many critics
20 of cloning via somatic cell nuclear transfer are concerned, however, that this initial presumption
21 of no interference with individual actions will lead to unwise policies.

22 Some considerations carry more weight in the public policy arena than they do in the
23 formation of individual judgments. In setting public policy, for example, pragmatic and
24 procedural considerations often, quite appropriately, carry greater weight than in deciding private
25 choices. One reason for this is that the burden of enforcing public policies must be considered.
26 For example, it is extremely intrusive to monitor reproductive decisions by individuals and
27 couples. It may be impractical to have a policy that allows some cases of somatic cell nuclear
28 transfer to create a child, while prohibiting others, even though we make such judgments
29 privately about individual actions. Furthermore, attempts to distinguish acceptable from
30 unacceptable reasons will be presumptuous and might lead people to misrepresent their true
31 reasons to fit the acceptable criteria.

32 Moreover, the reasoning used to evaluate the desirability of proposed public policies
33 regarding the creation of children through somatic cell nuclear transfer differs somewhat from
34 the reasoning employed in making private decisions. When individuals make judgments they
35 may rely on many sources of wisdom and knowledge, including their religious faith and moral
36 intuitions. People will use their understanding of morality to decide what they should and should
37 not do, as well as to judge the actions of others.