Within 2 years of the announced birth in 1997 of Dolly, the lamb cloned from the mammary cells of an adult ewe, research groups announced that they had cloned mice and calves by using differentiated somatic cells (1–3). In the cloning technique used to produce Dolly, the nucleus of a somatic cell of the ewe was transferred to a sheep oocyte from which the nucleus had been removed, and the cells were fused through electrofusion to produce offspring that shared the genome of the original ewe. Research into the science of reproductive somatic cell nuclear transfer (SCNT) is proceeding as investigators clone additional species by using the original and related methods.

The prospect of using reproductive SCNT to produce human beings has evoked extensive debate among lawmakers, academicians, religious leaders, international and national agencies, professional societies, and others. Whether human reproductive SCNT will ever be undertaken will depend on such factors as the safety and efficacy of the procedure, presence or absence of governmental regulation, perceptions of procreative rights, adherence to a voluntary moratorium against human cloning, consumer interest, and the intensity and extent of ethical objections. Reproductive SCNT in laboratory animals has heretofore been inefficient in that relatively few births have resulted from many attempts. It also has been associated with harmful side effects in calves and with high fetal and neonatal death rates (4, 5). Although concerns about fetal and neonatal safety alone would make reproductive SCNT unethical for humans at present, improvements in animal cloning indicate that safety concerns may be only a temporary barrier to reproductive SCNT in humans. Moreover, researchers have proposed using SCNT to generate embryonic stem cells for persons who need tissue or organ transplants, which raises issues not addressed in this report (6). If undertaken, the development of SCNT for such therapeutic purposes, in which embryos are not transferred for pregnancy, is likely to produce knowledge that could be used to achieve reproductive SCNT (7).

Although consensus about the ethical acceptability of reproductive SCNT does not and may never exist, it is appropriate to think prospectively about the ethical issues that reproductive SCNT would raise if preclinical data suggested the procedure were safe and effective and researchers sought to conduct human trials (8). Ongoing debates about the ethics of reproductive SCNT have revealed that some observers regard human reproductive SCNT as morally unacceptable in all circumstances, others see merit in reproductive SCNT in certain circumstances, and still others await more information before making judgments about the ethical status of the procedure.

REPRODUCTIVE SCNT AS UNETHICAL

One position holds that reproductive SCNT is unethical in all situations. This belief has contributed to the passage of restrictive laws in several nations and to proposals for restrictive legislation in the United States. According to this perspective, reproductive SCNT violates deeply cherished values and traditions. With natural conception or forms of assisted reproduction other than reproductive SCNT, a child is conceived through the mixing of two lineages. With reproductive SCNT, on the other hand, a child would be created in an asexual procedure and would be given a known genome. This represents a dramatic departure
from natural or assisted conception, and it can be compared with the production of a child to serve the needs of adults. Under this view, reproductive SCNT is more accurately seen as a form of replication than of reproduction (9).

According to this perspective, reproductive SCNT would devalue the genetic distinctiveness of each individual. It would deprive the child of a sense of mystery or right to ignorance about his or her origin (9). Moreover, it would amount to unethical experimentation on the child, who cannot consent to be conceived in a manner that poses risks to her or his health throughout life that cannot completely be addressed. For those who subscribe to this perspective, no situation would justify reproductive SCNT because the act itself is considered immoral. Some of those who object to reproductive SCNT believe that reservations about human cloning should be respected as a barometer of what is intuitively unacceptable (10).

**REPRODUCTIVE SCNT AS ETHICAL**

Another position defends the use of reproductive SCNT in medically based circumstances, provided that the safety of the procedure can be guaranteed (11, 12). According to this perspective, reproductive SCNT differs only in degree from other assisted reproductive technologies, and it is ethically defensible for two groups of patients: infertile couples who cannot otherwise be treated and couples at risk of passing a serious genetic disease on to their children. In the case of infertile couples, in which one or neither partner can produce gametes, two situations might apply. If the male partner cannot reproduce with his spermatozoa, reproductive SCNT with his somatic cell would enable him to have a genetic tie with the child. His partner would have a biological tie if she donates the recipient oocyte or gestates the child. If the female partner cannot reproduce with her ova, transferring the nuclear DNA from her somatic cell to an enucleated donor oocyte would allow her to have a genetic relation to the child, although her partner would not. In these situations, reproductive SCNT would allow infertile couples to conceive children who are genetically related to them, a reason that couples seek ART services. According to this perspective, reproductive SCNT would meet an infertile couple’s desire to participate biologically in the development of a new human being, and it could nurture the emotional bond between the partners. If conceiving a child with the genes of at least one partner is highly important for infertile couples, or if they have reservations about using the gametes of anonymous donors, reproductive SCNT would be a welcome alternative.

In the case of couples at genetic risk, reproductive SCNT could be used to avoid passing a serious genetic disease on to their offspring. If both the male and female partners are carriers of autosomal-recessive disease traits, one partner’s somatic cell could be used to conceive. If one partner has an autosomal-dominant disease, the unaffected partner’s somatic cell could be used. Reproductive SCNT would offer an alternative for at-risk couples who decline to transfer only unaffected embryos after preimplantation genetic diagnosis or to terminate a pregnancy after prenatal testing and a positive result for the disease in question.

**REPRODUCTIVE SCNT AS ETHICALLY UNCERTAIN**

Other perspectives fall somewhere between the positions discussed above. Persons who withhold judgment about reproductive SCNT pending further information generally presume that reproductive SCNT is unethical at present because of the risks posed to the fetus and child, but they are not yet ready to approve or bar the procedure (5). They voice concern about the potential impact of reproductive SCNT on offspring, families, and society, and they are as yet unpersuaded that reproductive SCNT would serve a valid family or reproductive need.

**Impact on Children**

If reproductive SCNT were available, its impact on offspring would presumably vary depending on family dynamics and other features of each situation. The effect could be inconsequential, or it could be positive if the child proudly shared the genome of a beloved parent and enjoyed a special kinship with that parent. Although the child would share the parent’s nuclear DNA, the child would be an individual in his or her own right because the child would experience unique circumstances of gestation, rearing, and education. In addition, the child would grow in a singular uterine environment and inherit the mitochondrial DNA of the oocyte donor. Barring unforeseen effects resulting from the use of an adult genome, such as premature aging, reproductive SCNT would probably produce a healthy child if healthy adults were somatic cell donors (13).

The effect of reproductive SCNT may also be harmful for children. Despite counseling to the contrary, rearing parents might harbor undue expectations about the child’s personality or believe that the child should be identical to the somatic cell donor. This risk is more likely if a fertile couple sought reproductive SCNT to replicate a person’s genome because the couple values the donor’s genetic traits, but it is also a risk if reproductive SCNT were used by infertile couples. In either case, harmful typecasting might result. Reproductive SCNT might also give children who know the traits of their genome donors too much information or unrealistic expectations about the future, which would be an especially acute problem if the older cell source had a genetic illness. If no limits were placed on the justifications for SCNT or on those who might act as genome sources, the issues could multiply. Separate issues would arise if the child were conceived with the cell of an existing child, deceased child or adult, living relative, or anonymous donor. Although the impact on the
child in each situation is unknown, the prospect of unfair pressures and expectations that would hinder the child’s emotional growth underscores the importance of considering the child’s interests in forging a unique identity when weighing the ethical acceptability of reproductive SCNT.

**Impact on Couples and Families**

Another set of issues involves the impact of reproductive SCNT on couples and families. The birth of a long-awaited child for couples experiencing infertility or genetic risk might have positive effects in families in which genetic relatedness is highly valued. On the other hand, reproductive SCNT would create the new relationship of a person being raised by a genetic twin who is also the social parent. Although this need not be injurious, the birth of a child who shares the genome of one parent might contribute to feelings of inadequacy among siblings who do not share a parent’s genome or feelings of superiority by the child who does.

A situation in which partners have different degrees of genetic relatedness to a child may or may not be troublesome. This is not unlike situations in which a family’s children have different genetic backgrounds because of remarriage or conception with gamete donation. This new possibility, however, underscores the unknown impact of reproductive SCNT on the family. Reproductive SCNT also raises questions about who is related to whom and about privileges and responsibilities in the event of divorce. Although these outcomes could be addressed through contract or legislation, they would raise additional complications beyond those that exist in gamete donation, embryo freezing, and surrogacy.

Additional concerns would arise if the procedure were widely used in various settings. Reproductive SCNT might be sought by fertile persons who lack a reproductive partner and prefer not to use donor gametes. Individual persons or couples who have no medically based reason for using reproductive SCNT might seek the technique to select a particular somatic cell donor with traits they admire. Depending on the numbers of procedures performed, SCNT might have unsettling effects on relations between the sexes and on families if people had the option of not combining their genes with those of another person. Although some see procreation by unmarried persons as a welcome and justified extension of procreative liberty, others are dismayed by what they perceive as the erosion of the two-parent family. Widely accessible reproductive SCNT might accelerate this erosion.

**Impact on Society**

If SCNT were limited only to couples who were infertile or at genetic risk, it might be done so infrequently as to have little societal impact. Demand for what would likely be a labor-intensive and costly procedure might be low, especially given advances in other forms of infertility treatment.

On the other hand, there is no guarantee that the use of reproductive SCNT would be carefully constrained. Its use on a broad scale would touch fundamental values that would warrant careful exploration before any clinical application is attempted. An often expressed concern is that prospective parents would seek somatic cell donors on the basis of their exemplary traits and that potential donors would market themselves as high-caliber genome sources. The seeking and offering of genomes might introduce an additional element of marketing to procreation. The eugenic practice of deliberately seeking persons who are perceived to be superior gene sources might promote a genetic determinism that devalues the unique capacity of each individual for personal growth. Reproductive SCNT might also perpetuate an undue emphasis on genetic relatedness. If done on a wide scale, some suggest, it could restrict genetic diversity and impair the ability of humans to adapt to a changing environment (14).

**SUMMARY**

Given the breadth and intensity of ethical concerns expressed globally about reproductive SCNT, it is important that caution be exercised before clinical use of this procedure is considered, even if safety concerns are adequately addressed. Even if a successful argument could be made for reproductive SCNT in particular situations, it is not clear that offering reproductive SCNT generally would be justified. Nevertheless, it does not necessarily follow that the procedure should be foreclosed permanently. There is not yet clear consensus that reproductive SCNT in cases of infertility serves a compelling need. If there were, additional problems would still need to be addressed, such as the need for counseling of couples and decisions about what to disclose to the child. Nor is there clear consensus on a compelling need to bar the technique.

As long as the safety of reproductive SCNT is uncertain, ethical issues have been insufficiently explored, and infertile couples have alternatives for conception, the use of reproductive SCNT by medical professionals does not meet standards of ethical acceptability. This situation does not, however, preclude research into therapeutic SCNT that does not involve transferring embryos to the uterus, provided that ethical procedures for conducting research are followed (15). Nor does a moratorium on reproductive SCNT remove the need to study more carefully the ethical implications of cloning, especially for infertile couples.

**References**


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**SUMMARY**

Given the breadth and intensity of ethical concerns expressed globally about reproductive SCNT, it is important that caution be exercised before clinical use of this procedure is considered, even if safety concerns are adequately addressed. Even if a successful argument could be made for reproductive SCNT in particular situations, it is not clear that offering reproductive SCNT generally would be justified. Nevertheless, it does not necessarily follow that the procedure should be foreclosed permanently. There is not yet clear consensus that reproductive SCNT in cases of infertility serves a compelling need. If there were, additional problems would still need to be addressed, such as the need for counseling of couples and decisions about what to disclose to the child. Nor is there clear consensus on a compelling need to bar the technique.

As long as the safety of reproductive SCNT is uncertain, ethical issues have been insufficiently explored, and infertile couples have alternatives for conception, the use of reproductive SCNT by medical professionals does not meet standards of ethical acceptability. This situation does not, however, preclude research into therapeutic SCNT that does not involve transferring embryos to the uterus, provided that ethical procedures for conducting research are followed (15). Nor does a moratorium on reproductive SCNT remove the need to study more carefully the ethical implications of cloning, especially for infertile couples.
Two methods might be used to produce embryonic stem cells that are genetically identical to the cells of individual patients. One method would be to create an embryo through SCNT with the patient’s nucleus and derive embryonic stem cells from that embryo. These cells would then be coaxed to differentiate into specifically needed tissues or organs for transplantation to the somatic cell donor. A second method would be to transfer the patient’s somatic cell nucleus to a previously obtained embryonic stem cell and derive an embryonic stem cell line from that. In either case, SCNT would be used to create cells that are compatible with the patient’s immunologic system. This would theoretically eliminate the need for antirejection drugs.

The distinction between reproductive and therapeutic cloning appears in public commentary to point out that the SCNT procedure can be used for different ends, each of which raises separate issues (Gurdon JB, Colman A. The future of cloning. Science 1999;402:743–6). Use of reproductive SCNT and therapeutic SCNT in the present paper does not imply that these terms are acceptable scientific terminology.

Reproductive SCNT differs from embryo splitting, which has resulted in the live births of rhesus monkeys and other mammals (Chan AWS, Dominko T, Luetjens CM, Neuber E, Martinovich C, Hewitson L, et al. Clonal propagation of primate offspring by embryo splitting. Science 2000;287:317–9). In embryo splitting, which is hypothetical for humans, the blastomeres of embryos would be separated to increase the number of embryos available for IVF. The Ethics Committee concluded in an earlier paper that research into embryo splitting to improve the efficacy of IVF treatments for infertility would be ethically acceptable (Ethics Committee of the American Society for Reproductive Medicine. Ethical considerations of assisted reproductive technologies. Fertil Steril. 1997;67(Suppl 1):4S–5S).


