I, CLONE

Sometime, somewhere, someone will generate a cloned human being. What will happen then? **By Ronald M. Green**

DAN WAGNER

WITHIN THE FIRST FIVE years of the next century, a team of scientists somewhere in the world will probably announce the birth of the first cloned human baby. Like Louise Brown, the first child born as the result of in vitro fertilization 21 years ago, the cloned infant will be showered with media attention. But within a few years it will be just one of hundreds or thousands of such children around the world.

It has been possible to envision such a scenario realistically only since Ian Wilmut and his colleagues at the Roslin Institute near Edinburgh, Scotland, announced in February 1997 that they had cloned a sheep named Dolly from the udder cells of a ewe. The technique used by Wilmut and his co-workers—a technology called somatic-cell nuclear transfer—will probably be the way in which the first human clone will be created.

In somatic-cell nuclear transfer, researchers take the nucleus—which contains the DNA that comprises an individual's genes—of one cell and inject it into an egg, or ovum, whose own nucleus has been removed. The resulting embryo, which will carry the nucleus donor's DNA in every one of its cells, is then implanted into the womb of a female and carried to term.

Such research on the basic processes of cell differentiation holds out the promise of dramatic new medical interventions and cures. Burn victims or those with spinal cord injuries might be provided with replacement skin or nerve tissue grown from their own body cells. The damage done by degenerative disorders such as diabetes, Parkinson's disease or Alzheimer's disease might be reversed. In the more distant future, scientists might be able to grow whole replacement organs that our bodies will not reject [see "Embryonic Stem Cells for Medicine," on page 18].

These important medical uses of cloning technology urge us to be careful in our efforts to restrict cloning research. In the immediate wake of Dolly, politicians around the world proposed or implemented bans on human cloning. In the U.S., President Bill Clinton instituted a moratorium on federal funding for human cloning experiments, and the National Bioethics Advisory Commission urged that the ban be extended to private-sector research as well. Congress continues to study various proposals for enacting such a total ban.

In view of the still unknown physical risks that cloning might impose on the unborn child, caution is appropriate. Of the 29 early embryos created by somatic-cell nuclear transfer and implanted into various ewes by Roslin researchers, only one, Dolly, survived, suggesting that the technique currently has a high rate of embryonic and fetal loss. Dolly herself appears to be a normal three-year-old sheep—she recently gave birth to triplets following her second pregnancy. But a recent report that her telomeres—the tips of chromosomes, which tend to shrink as cells grow older—are shorter than normal for her age suggests that her life span might be reduced. This and other matters must be sorted out and substantial further animal research will need to be completed before cloning can be applied safely to humans.

Eventually animal research may indicate that human cloning can be done at no greater physical risk to the child than IVF posed when it was first introduced. One would hope that such research will be done openly in the U.S., Canada, Europe or Japan, where established government agencies exist to provide careful oversight of the implications of the studies for human subjects. Less desirably, but more probably, it might happen in clandestine fashion in some offshore laboratory where a couple desperate for a child has put their hopes in the hands of a researcher seeking instant renown.

Given the pace of events, it is possible that this researcher is already at work. For now, the technical limiting factor is the availability of a sufficient number of ripe human eggs. If Dolly is an indication, hundreds might be needed to produce only a few viable cloned embryos. Current assisted-reproduction regimens that use hormone injections to induce egg maturation produce at best only a few eggs during each female menstrual cycle. But scientists might soon resolve this problem by improving ways to store frozen eggs and by developing methods for inducing the maturation of eggs in egg follicles maintained in laboratory culture dishes.

It is possible that a **researcher** somewhere in the world is **already at work** on a **human clone**.

Although human cloning could generate a troop of people who look just like you, the clones won't be your age unless they were cloned right after you were conceived. They will still have to grow through childhood and adolescence to adulthood. The big question is: Will society regard them as separate individuals?

WHO FIRST?

Once human cloning is possible, why would anyone want to have a child that way? As we consider this question, we should put aside the nightmare scenarios much talked about in the press. These include dictators using cloning to amass an army of "perfect soldiers" or wealthy egotists seeking to produce hundreds or thousands of copies of themselves. Popular films such as *Multiplicity* feed these nightmares by obscuring the fact that cloning cannot instantaneously yield a copy of an existing adult human being. What somatic-cell nuclear transfer technology produces are cloned human embryos. These require the labor- and time-intensive processes of gestation and child rearing to reach adulthood. Saddam Hussein would have to wait 20 years to realize his dream of a perfect army. And the Donald Trumps of the world would also have to enlist thousands of women to be the mothers of their clones.

For all their efforts, those seeking to mass-produce children in this way, as well as others who seek an exact copy of someone else, would almost certainly be disappointed in the end. Although genes contribute to the array of abilities and limits each of us possesses, from conception forward their expression is constantly shaped by environmental factors, by the unique experiences of each individual and by purely chance factors in biological and social development. Even identical twins (natural human clones) show different physical and mental characteristics to some degree. How much more will this be true of cloned children raised at different times and in different environments from their nucleus-donor "parent"? As one wit has observed, someone trying to clone a future

Adolf Hitler might instead produce a modestly talented painter.

So who is most likely to want or use human cloning? First are those individuals or couples who lack the gametes (eggs or sperm) needed for sexual reproduction. Since the birth of Louise Brown, assisted-reproduction technologies have made remarkable progress in helping infertile women and men become parents. Women with blocked or missing fallopian tubes, which carry the eggs from the ovaries to the womb, can now use in vitro fertilization to overcome the problem, and those without a functional uterus can seek the aid of a surrogate mother. A male who produces too few viable sperm cells can become a father using the new technique of intracytoplasmic sperm injection, which involves inserting a single sperm or the progenitor of a sperm cell into a recipient egg.

Despite this progress, however, women who lack ovaries altogether and men whose testicles have failed to develop or have been removed must still use donor gametes if they wish to have a child, which means that the child will not carry any of their genes. Some of these individuals might prefer to use cloning technology to have a genetically related child. If a male totally lacks sperm or the testicular cells that make it, a nucleus from one of his body cells could be inserted into an egg from his mate that had had its nucleus removed. The child she would bear would be an identical twin of its father. For the couple's second child, the mother's nucleus could be used in the same procedure.

One very large category of such users of cloning might be lesbian couples. Currently if two lesbians wish to have a child, they must use donor sperm. In an era of changing laws about the rights of gamete donors, this opens their relationship to possible intervention by the sperm donor if he decides he wants to play a role in raising the child. Cloning technology avoids this problem by permitting each member of the pair to bear a child whose genes are provided by her partner. Because the egg-donor mother also supplies to each embryo a small number of mitochondria—tiny energy factories within cells that have some of their own genetic material—this approach even affords lesbian couples an approximation of sexual reproduction. (Cloning might not be used as widely by gay males, because they would need to find an egg donor and a surrogate mother.)

A second broad class of possible users of cloning technologies includes individuals or couples whose genes carry mutations that might cause serious genetic disease in their offspring. At present, if such people want a child with some genetic relationship to themselves, they can substitute donated sperm or eggs for one parent's or have each embryo analyzed genetically using preimplantation genetic diagnosis so that only those embryos shown to be free of the disease-causing gene are transferred to the mother's womb. The large number of genetic mutations contributing to some disorders and the uncertainty about which gene mutations cause some conditions limit this approach, however.

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Some couples with genetic disease in their families will choose cloning as a way of avoiding what they regard as "reproductive roulette." Although the cloned child will carry the same problem genes as the parent who donates the nucleus, he or she will in all likelihood enjoy the parent's state of health and will be free of the additional risks caused by mixing both parents' genes during sexual reproduction. It is true, of course, that sex is nature's way of developing new combinations of genes that are able to resist unknown health threats in the future. Therefore, cloning should never be allowed to become so common that it reduces the overall diversity in the human gene pool. Only a relatively few couples are likely to use cloning in this way, however, and these couples will reasonably forgo the general advantages conveyed by sexual reproduction to reduce the immediate risks of passing on a genetic disease to their child.

Cloning also brings hope to families with inherited genetic diseases by opening the way to gene therapy. Such therapy—the actual correction or replacement of defective gene sequences in the embryo or the adult—is the holy grail of genetic medicine. To date, however, this research has been slowed by the inefficiency of the

RODDY FIELD *Roslin Institute*

Cloning seems to have no ill effects so far. Dolly, the first mammal ever to be cloned, gave birth in 1998 to Bonnie, who by all accounts is normal. This past year Dolly delivered a healthy set of triplets.

ROBERT HOLMES *Corbis*

Cloning will allow lesbian mothers to give birth to a clone of their partner. Gay men would still have to find an egg donor and a surrogate mother.

viruses that are now used as vectors to carry new genes into cells. By whatever means they are infused into the body, such vectors seem to reach and alter the DNA in only a frustratingly small number of cells.

Cloning promises an end run around this problem. With a large population of cells from one parent or from an embryo created from both parents' gametes, vectors could be created to convey the desired gene sequence. Scientists could determine which cells have taken up the correct sequence using fluorescent tags that cause those cells to glow. The nucleus of one of these cells could then be inserted into an egg whose own nucleus has been removed, and the "cloned" embryo could be transferred to the mother's womb. The resulting child and its descendants would thereafter carry the corrected gene in every cell of their bodies. In this way, age-old genetic maladies such as Tay-Sachs disease, cystic fibrosis, muscular dystrophy or Huntington's disease could be eliminated completely from family trees.

CLONING AND IDENTITY

Merely mentioning these beneficial uses of cloning raises difficult ethical questions. The bright hope of gene therapy is dimmed somewhat by the reawakening of eugenic fears. If we can manipulate embryos to prevent disease, why not go further and seek "enhancements" of human abilities? Greater disease resistance, strength and intelligence all beckon alluringly, but questions abound. Will we be tampering with the diversity that has been the mainstay of human survival in the past? Who will choose the alleged enhancements, and what will prevent a repetition of the terrible racist and coercive eugenic programs of the past?

Even if it proves physically safe for the resulting children, human cloning raises its own share of ethics dilemmas. Many wonder, for example, about the psychological well-being of a cloned child. What does it mean in terms of intrafamily relations for someone to be born the identical twin of his or her parent? What pressures will a cloned child experience if, from his or her birth onward, he or she is constantly being compared to an esteemed or beloved person who has already lived? The problem may be more acute if parents seek to replace a deceased child with a cloned replica. Is there, as some ethicists have argued, a "right to one's unique genotype," or genetic code—a right that cloning violates? Will cloning lead to even more serious violations of human dignity? Some fear that people may use cloning to produce a subordinate class of humans created as tissue or organ donors.

Some of these fears are less substantial than others. Existing laws and institutions should protect people produced by cloning from exploitation. Cloned humans could no more be "harvested" for their organs than people can be today. The more subtle psychological and familial harms are a worry, but they are not unique to cloning. Parents have always imposed unrealistic expectations on their children, and in the wake of widespread divorce and remarriage we have grown familiar with unusual family structures and relationships. Clearly, the initial efforts at human cloning will require good counseling for the parents and careful follow-up of the children. What is needed is caution, not necessarily prohibition.

As we think about these concerns, it is useful to keep a few things in mind. First, cloning will probably not be a widely employed reproductive technology. For many reasons, the vast majority of heterosexuals will still prefer the "old-fashioned," sexual way of producing children. No other method better expresses the loving union of a man and a woman seeking to make a baby.

Second, as we think about those who would use cloning, we would do well to remember that the single most important factor affecting the quality of a child's life is the love and devotion he or she receives from parents, not the methods or circumstances of the person's birth. Because children produced by cloning will probably be extremely wanted children, there is no reason to think that with good counseling support for their parents they will not experience the love and care they deserve.

What will life be like for the first generation of cloned children? Being at the center of scientific and popular attention will not be easy for them. They and their parents will also have to negotiate the worrisome problems created by genetic identity and unavoidable expectations. But with all these difficulties, there may also be some novel satisfactions. As cross-generational twins, a cloned child and his or her parent may experience some of the unique intimacy now shared by sibling twins. Indeed, it would not be surprising if, in the more distant future, some cloned individuals chose to perpetuate a family "tradition" by having a cloned child themselves when they decide to reproduce.

ABOUT THE AUTHOR

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