

Telomeres and the Ethics of Human Cloning

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Abstract

In search of a potential problem with cloning, I investigate the phenomenon of telomere shortening which is caused by cell replication; clones created from somatic cells will have shortened telomeres and therefore reach a state of senescence more rapidly. While genetic intervention might fix this problem at some point in the future, I ask whether, absent technological advances, this biological phenomenon undermines the moral permissibility of cloning.

Telomeres and Aging

James Watson, who, along with Francis Crick, discovered the famed double-helix structure of DNA, also observed that polymerases (which copy DNA) are unable to begin the transcription process at the very end of a DNA strand. Rather, transcription must begin *within* the genetic code and, consequently, the end is not replicated. If the DNA that was not replicated possessed valuable genetic data, then this would obviously be quite bad; each successive replication would delete part of our genome. But, as it turns out, natural selection found a clever way around this problem. At the end of a strand of DNA, we (and all other living organisms) are endowed with telomeres which are like the protective aglets on the ends of shoelaces; the telomere serves no function other than to protect our genome against the imperfection of polymerases. Given that our polymerases fail to replicate some segment on the end of our genome, it is obviously better that those segments are non-coding DNA than valuable genes.

Each time a cell divides and the genetic material in the cell nucleus is copied, the telomere shortens as the polymerase copies only (an interior) part of the chromosomes. Telomeres, while long, are nevertheless constantly growing shorter. Interestingly, telomeres only shorten in somatic cells (e.g., hair, skin, etc.), and not in germ line (e.g., sperm and egg) cells. Why? Humans have a gene (on the fourteenth chromosome) called TEP1 which codes for the production of a protein that forms part of a "biological machine" called telomerase (Ridley 2000). Though the process is not yet fully understood, telomerase repairs shortened telomeres by re-lengthening them. In most human tissues, the genes that create telomerase are deactivated which consequently preordains the shortening of telomeres. In germ line cells, however, the genes for telomerase are not deactivated. (Notably, malignant cancer cells reactivate the telomerase genes, a process which allows the cancer to reproduce without telomere shortening.)

Why does any of this matter? There is little controversy that telomere shortening is the central reason that cells grow old and die—cell division stops once the telomeres become sufficiently short and the cells consequently begin to senesce. But there are also good reasons to think that the shortening of telomeres is one of the reasons that the entire organism ages (and dies); research has also shown that this sort of cellular aging can lead to degenerative dis-

eases and conditions. For example, the chromosomes in arterial cells typically have shorter telomeres than the chromosomes in venous cells. This is no doubt because arterial cells are under higher pressures and become damaged more often; consequently, they have to repair themselves, which involves cell copying and telomere shortening. Arterial cells therefore reach a state of senescence faster than venous cells, which is why we die from arterial hardening rather than venous hardening (Chang and Harley 1995).

Despite these findings, there are certainly causes of senescence other than the shortening of telomeres. Rather, it is far more likely that telomere shortening is *one* of the contributing factors to senescence, of which there are likely to be many (Austad 1997).¹ Therefore, I grant that telomere shortening is not the only factor that contributes to aging. Nevertheless, it is uncontroversial to claim that telomere shortening leads to aging (on both the cellular and organism levels), and that the relationship between telomeres and aging is quite important.

It should also be observed that the prospect of genetic engineering could solve the problem of telomere shortening: if it becomes possible to reactivate telomerase (or insert genes that create it), organisms will be able to repair frayed telomeres and cells will be, at least theoretically, immortal. The Geron Corporation (www.geron.com), for example, has done extensive research on telomeres and telomerase and has been able to insert genes for telomerase into cells that otherwise lacked those genes; the cells were then able to divide indefinitely. Whether an active telomerase gene is inserted or whether the current deactivated ones can be reactivated, science offers the hope of being able to respond to senescence induced by telomere shortening. What is equally exciting is that this research is likely to also yield ways to deactivate the telomerase in cancers which would consequently limit cancerous growth. Despite a cautious optimism on these fronts, it is not currently technologically possible to engineer wide-scale reactivation of telomerase in the human body (or to insert the gene which would code for telomerase production), nor is it likely that this breakthrough will come in the immediate future. So, for the moment, we are stuck with senescence once our cells cease to replicate.

Cloning

Now, we can consider cloning. Though the point may now be obvious, allow me to make it explicit. Imagine that a thirty-year old woman wished to create a genetic clone. She would have to acquire a denucleated egg and insert the nucleus from one of her *somatic* cells (remember that germ-line nuclei have unpaired chromosomes) into this egg. The DNA contained within the nucleus of her somatic cell would have shortened telomeres because it would have been generated after several generations of cellular replication. The clone would therefore *begin* its existence with shortened telomeres; its constitutive cells would have fewer replications in their futures than those of a zygote created by germ line cells whose telomeres would have been re-lengthened by telomerase. The clone would therefore senesce more rapidly (or, perhaps more accurately, *earlier*) than a child conceived through sexual reproduction and this senescence would result in heightened susceptibility to degenerative conditions and diseases, as well as shortened life expectancy (Associated Press 2003).²

What sorts of normative conclusions can be informed by this biological consideration? It seems obvious that there is at least something wrong/bad/undesirable with cloning given these consequences, but what is it? Laura Purdy has argued that reproduction is immoral if the child will not lead a “minimally satisfying life”; she argues that this criterion can be defended on either a consequentialist or contractarian approach (Purdy 2000). Accepting Purdy’s suggestion, we could ask whether cloning would be immoral given the biological considerations that we have been discussing. Clearly there is no reason to think that a clone with shortened telomeres would fail to have a minimally satisfying life. His life would be comparatively less desirable than a “normal” life in virtue of an earlier onset of senescence and, presumably, a shortened life span, but it is wildly implausible to think that this life would not be one worth living (especially from the point of view of the clone).

Another potential response would be to argue that cloning *harms* the clone by subjugating him to various undesirable propensities (such as earlier onset of degenerative conditions). Some philosophers have argued against the logical coherence of this notion (as applied to “wrongful birth” more generally), and it is instructive to look at the argument. One plausible account of harm is to apply a counterfactual (or comparative) criterion: X harms Y by doing A if Y would be better off had X not done A (Parfit 1984; Kagen 2002). For example, I harm my friend by kicking him because he would have been better off had I not kicked him. While this account of harm is not perfect (there are problems with over-determination), it is certainly one that is widely considered and constitutes the starting point for many “advanced” versions (Nagel 1979; McMahan 2002). So, we could ask, does cloning harm the clone? If so, the clone would have to have been better off *had cloning not taken place*. However, this condition can obviously not be met; had cloning not taken place, the clone would not exist at all, much less have a higher level of overall welfare. Therefore, cloning cannot harm the

clone (Parfit 1986; Robertson 1994).³ While some non-comparative accounts of harm have been proposed (Shiffrin 1999; Woodward 1986), I nevertheless take the received view to be consistent with the general spirit (if not the details) of the above proposal. Therefore, I think it is fairly uncontentious to *deny* that cloning harms the clone.

Nonetheless, we could adopt an impersonal comparative account, which would hold that cloning is wrong because the life of a clone would be worse (in some way) than that of a non-clone.⁴ Parfit, for example, proposes *The Same Number Quality Claim* (Q): “If in either of two outcomes the same number of people would ever live, it would be bad if those who live are worse off, or have a lower quality of life, than those who would have lived” (Parfit 1986).⁵ To take his example, consider a fourteen year-old girl who chooses to have a child now rather than wait until she would be able to provide a better life for the child. Insofar as it is metaphysically impossible for *that* child to have been born substantially later, we must locate the wrongness of the girl’s act not in its effect upon *that* child, but rather in the fact that she *could* have created *some* child with higher welfare had she waited.

I think that Parfit’s line here is extremely compelling. Turning back to cloning, we might apply (Q).⁶ If parents were to have children, we might think that they should produce the children, to the best of their ability, that would be maximally well off. Children would obviously be better off being born with normal, as opposed to stunted telomeres, so parents should do whatever they can to avoid this problem. Obviously sexual reproduction would not transfer shortened telomeres to offspring so, all else being equal, sexual reproduction is (for now) better than cloning.

But for many of those who would consider cloning, sexual reproduction is not an option. We might, for example, imagine a single person, a sterile couple, or a homosexual couple who is trying to reproduce. In these cases, is cloning morally permissible? If we take Parfit’s principle seriously, cloning would only be morally permissible if it were to maximize the welfare of the potential offspring. *If*, for example, the option were to clone or to not reproduce, then cloning would still be morally permissible so long as the clonant would live a minimally satisfying life (which, I think, we have every reason to believe that s/he would).

But, more likely, there would other options. For example, we can wait to see whether genetic engineering will be able to reactivate telomerase in somatic cells or to insert a gene that would code for its production. If the technologies do develop, then we could have cloning without moral hazards. Given the potential risks of cloning now and their potential abatement at some time in the future, it seems that we should wait and see if science can fulfill its potential. Alternatively, prospective cloners might seek sperm or egg donation for sexual reproduction. If one parent is sterile, the other could reproduce sexually with a third party (through IVF, of course). Similar options would be available for single parents or homosexual couples, though males would obviously need to obtain gestational surro-

gates (which is not without moral problems).

While I am inclined to support Parfit's principle, I nevertheless have one concern. Namely, I worry that a full endorsement of (Q) might serve as an indictment against all sub-optimal reproductions; this indictment would follow from a commitment to any maximizing consequentialism. For example, my daughter might be worse off given her acquisition of half of my wife's genes than a daughter that could have been created had I mated with someone who was more genetically fit. Does this mean that it was wrong to reproduce with my wife as opposed to someone else? I would certainly want to resist this conclusion.

Perhaps, however, the consequentialist need not have this commitment: it is certainly plausible to think that utility is not maximized if reproductions aimed solely at maximizing the welfare of the child. If every reproduction were to be certified (either morally or legally) as maximizing the welfare of the child, there would be obvious effects upon the relationships of the parents, the relationships between the parents and the children, etc. If, for example, my wife were to inform me that "our" child's welfare would be maximized if she were to be inseminated by a donor (of high genetic worth) rather than reproducing with me, there could obviously be negative effects. So, while we might grant that, *prima facie*, the welfare of children should be maximized, there might be significant countervailing considerations that would allow for reproductions which would not maximize the welfare of the child.⁷ Finally, it is worth observing that the consequentialist approach would only commit parents to producing the best children that they were *able* to. While many reproductions might be sub-optimal insofar as children's lives would not be maximally rewarding, we could nevertheless observe that the parents were constrained, to some extent, with the lives that they could offer their offspring.

Conclusion

In conclusion, I have suggested that there is a biological issue inherent in human cloning: the clonant will senesce earlier than someone who was created through sexual reproduction. While there is cause for cautious optimism that genetic engineering will be able to address this problem, the solution is, at best, still a few years away. Investigating the normative implications of this biological phenomenon, I proposed that we adopt an impersonal comparative approach, which would hold that we should reproduce so as to maximize the welfare of our offspring (to the best of our abilities). This is similar to principles argued for by Derek Parfit and Julian Savulescu and, hopefully, has intuitive resonance and conceptual appeal. It is unlikely that cloning (at the present time) will satisfy this criterion given the existence of alternative means of reproduction and/or given the potential technological developments in the future. Therefore, I suggest that we have located at least a *prima facie* problem with human cloning, though I grant that this problem is contingent upon scientific limitations that might dissolve.

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References

- Associated Press. 2004. Cloning pioneer Dolly put to death. 14 February.
- Austad, S. J. 1997. *Why We Age?* New York: John Wiley & Sons.
- Chang, E., and C. B. Harley. 1995. Telomere length and replicative aging in human vascular tissues. *Proceedings of the National Academy of Sciences of the U. S. A.* 92:11190-94.
- Kagen, S. 2002. *The Limits of Morality.* Oxford: Oxford University Press.
- Kass, L. 1997. The wisdom of repugnance. *New Republic* 216:17-26.
- McMahan, J. 2002. *The Ethics of Killing: Problems at the Margins of Life.* Oxford: Oxford University Press.
- Nagel, T. 1979. Death. In *Mortal Questions*, 1-10. Cambridge: Cambridge University Press.
- Parfit, D. 1986. *Reasons and Persons.* New York: Oxford University Press.
- Purdy, L. M. 2000. Genetics and reproductive risk: Can having children be immoral? In *Biomedical Ethics*, eds. T. A. Mappes and D. Degrazia. Boston: McGraw Hill.
- Ridley, M. 2000. *Genome: The Autobiography of a Species in 23 Chapters.* New York: Perennial.
- Roberts, M. 1996. Human cloning: A case of no harm done? *Journal of Medicine and Philosophy* 21:537-54.
- Robertson, J. A. 1994. *Children of Choice: Freedom and the New Reproductive Technologies.* Princeton: Princeton University Press.
- Savulescu, J. 2001. Procreative beneficence: Why we should select the best children. *Bioethics* 15:414-26.
- Shiffrin, S. 1999. Wrongful life, procreative responsibility, and the significance of harm. *Legal Theory* 5:117-48.
- Woodward, J. 1986. The non-identity problem. *Ethics* 96:804-31.

Notes

1 Genetic disposition is likely to be another substantial contributor to senescence. For example, George Martin, a geneticist and pathologist, has estimated that as many as 7,000 of our 100,000 genes may influence some aspect of our aging.

2 It should be said that this is *not* mere speculation: Dolly, the first mammalian clone, was euthanized after developing both lung cancer at an early age (as well as arthritis); scientists observed that she "had started to show signs of wear more typical of an older animal." (Most sheep live to be eleven to twelve years old, whereas Dolly lived to be six.)

3 Parfit argues that this consequence leads to the "non-identity problem": we cannot say that the decision to reproduce was worse *for that child* because, absent reproduction, that child would *not exist*. (Let's assume the child has a minimally satisfying life.) This line has also been taken by John Robertson in several articles, as well as in his book *Children of Choice: Freedom and the New Reproductive Technologies*. For a contrary view, see Melinda Robert's "Human Cloning: A Case of No Harm Done?"

4 This is, of course, a consequentialist approach that might not be supported by non-consequentialists. Nevertheless, the principle I offer will hopefully be benign enough so as to alienate very few people. Parfit does consider (and reject) deontic solutions.

5 See also Savulescu 2001; Savulescu proposes a similar principle of "procreative beneficence": "couples (or single reproducers) should select the child, of the possible children they could have, who is expected to have the best life, or at least as good a life as the others, based on the relevant, available information."

6 Similarly, we might apply Savulescu's principle of procreative beneficence; either principle will yield the same result.

7 Or, alternatively, we might reasonably think that a child's life would go better if he were to actually be related to both of his parents rather than score higher on some detached barometer of genetic fitness. Certainly an unrelated parent would not feel as close to a child as a related parent would; these feelings could be manifested as utility considerations. This response would also allay my concern.

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