Cloning: Scientific Technological & Ethical Considerations

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CLONING: SCIENTIFIC, TECHNOLOGICAL & ETHICAL CONSIDERATIONS

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Good morning to all. Interestingly, to begin, the term cloning comes from the Greek, clone, which refers to a twig. Now, by exact definition, cloning is the replication of an exact genetic copy of an organism via the use of somatic tissue or a cell from the donor organism.

Notice: this cloning is not new technology. For example, a horticulturist or a gardener have long known how to make genetically identical plants: use a twig of a plant, dip the end of the twig into some rooting medium, and place into soil. Within a few weeks, it's growing up as roots. Specifically, gardeners can do this with a geranium, and in the end, that new little plantlet is genetically identical to the donor plant that you got the twig originally from.

Similarly, as a second example, zoologists can do the same thing. They can chop one arm off of a starfish, and after a period of time, it will regenerate into a separate entity. However, this separate starfish will be genetically the same as the donor starfish that was the source of the original "donor" arm. My presentation is going to discuss first some of the methods of cloning, then related technology, and finally, the ethical issues involved in cloning.

First: I will discuss the methods of cloning that exist today. The two primary means to achieve cloning in animal life forms are: (1) embryo splitting and (2) nuclear transplantation. Note that nuclear transplantation also goes by the name Somatic Cell Nuclear Transfer.

* These remarks are an actual transcript of the author's comments at the St. John's Journal of Legal Commentary Symposium on Feb. 25, 2005.
As far as the first way to create a clone, what is embryo splitting? The embryo's cells will be removed and then properly cultivated at the very early stage - whether it's the two, four, or eight cell stage. These cells are referred to as "blastomeres," and each cell, at this particular stage, has "Totipotency." Totipotency is basically the property where the genetic material has not been programmed yet to develop into specific tissues or organs. As a result, that individual cell can be taken in the proper cultivation and used to create an individual organism, on and of its own. Take two cells, separate them; it works just like with identical twins, who are formed by the splitting of the embryo, usually, at the two or four cell stage.

The second way to clone is via nuclear transplantation. That method is a bit more difficult, because you have to perform the fusion of the nucleus of a body cell. That body cell can be taken from an adult organism or a fetal organism, and then that body cell is placed into an unfertilized egg. Now, notice the term "enucleated." The original nucleus of that unfertilized egg has to be removed before the nucleus of the donor cell can be inserted. Then the now-enucleated egg is stimulated, and the cell will undergo divisions and develop into an embryo. There is a challenge here, based on why we have to enucleate it. You have to get the nucleus at the cell's cycle phase prior to the "S phase." In essence, here is the basic premise of the whole thing: Nature hates too much or too little DNA. Humans have forty six chromosomes in all of our cells.¹ One chromosome more will result in developmental abnormalities. Example, Downs Syndrome individuals result from having one extra chromosome, chromosome 21. Or, having one chromosome X less in a female human, for example, results in an individual with Turner's Syndrome. Both yield developmental deformities.

If you take a look at the cell cycle, the fourth cell undergoes division. It has to go through a series of preparations before you will have one cell divided into two. The process of one cell dividing into two for body cells is called mitosis. After the cells have been divided, they are referred to as daughter cells, which will then have to go through a period of development of

expansion of mass and volume and specialization, perhaps. This is the "G1 phase." They may, then, develop and then go into a so-called idle phase, where they have active metabolic activity, but they are not going to go through any process of reproduction again. This is the "G0 phase."

But if the cell is stimulated or requires to be undergoing division, it then has to go through some preparation before the cell will actually divide. This is known as the "S phase," where a full copy of all DNA is made. Then there are the final preparations, where certain biochemical events occur in G2 and then finally the actual cell division occurs. The challenge that many in nuclear transplantation had was getting a nucleus that was not in "S phase," because once you start down that road, you have more DNA than you actually need, and that led to developmental difficulties or failures of the clone.

Now, there are certain advantages to animal cloning. Mind you, this is a different topic: animal cloning versus human cloning. One, the cloned transgenic animals can be used to make new pharmaceuticals. If you have a successful transgenic animal, you would like to expand the herd to expand, in essence, these biological manufacturing devices. They might be making blood clotting protein in their milk, or they might be making albumin that would be used for blood substitutes, et cetera. Well, the way to expand the herd quicker may be to clone the actual successfully transgenic animal.

Another use for this cloning is to restore the extinct or endangered species. This has gotten great interest in China, a nation which rejects human cloning, but which has moved forward with animal cloning to expand their rapidly diminished endangered species, the panda bear. Also, this technology can be used to expand the number of highly prized farm animals. Farmer Brown would love to have more of that prized cow making milk or that prized steer. As a matter of fact, the proverbial "Farmer Brown" could perhaps even profit from cloning of these animals, and thereby reaping returns on this years after the actual animals have been sent to the abattoir.

Finally, animal cloning also can provide genetically identical lab animals for research and drug studies. In certain drug studies, when a population of animals is undergoing the drug study, you might get some genetic variations within the animals that create unique symptoms, adverse effects, et cetera. There, the question is, is it the drug itself or is it the genetic variations that exist within the animals? If you had a population of cloned animals, cloned rats, for example, you could, then, give the drug, and then if there are adverse effects, then the evidence really suggests more that it is the drug itself, not genetic variation, and thereby, perhaps save individuals' lives down the road, by seeing ahead of time adverse effects that might show up with that particular pharmaceutical.

Moving on, there are, in fact, disadvantages of animal cloning. Genetic variation within a population enhances the survival of the species. Whenever you have a changing environment, global warming, global cooling, even decreases in the amount of oxygen dissolved in the water, there are going to be some changes within that population because of the generic variations within the population that will survive and live to the next day, thereby passing on their genes to the next generation. If you have a lot of the population being cloned, they all have genetic non-variation: they are all genetically similar. Therefore, the genetically similar animals are going to have a higher risk if some event occurs that wipes out a good amount of the species. In fact, it will wipe out all of the species.

Furthermore, by the way, variations in environment can include also the rise of new viruses, new bacteria, new diseases, et cetera. The other problem with animal cloning is that there is an absence of genetic repair. One of the challenges that have been noticed, for example, in some of the Dolly studies, was that Dolly, in essence, came forth with aged DNA. It was of the age from the donor. Therefore, as opposed to what happens in meiosis and fertilization where there is some repair occurring of the DNA, Dolly had shortened telomeres, which are the ends of the chromosomes, that indicated aging. Dolly subsequently died earlier than a normal sheep existence, which suggests that any

clone that might come forth would have a reduced life span based on the age of its donor that donated the nucleus.

Another shortcoming is that the technique for animal cloning has also not been perfected. All the studies have shown low success rates, well below ten percent. The primate species have been the most difficult to achieve success with cloning. Similarly, the sheep studies had less than one percent success rate with cloning. The best rates were probably in mouse studies, which had a two point eight percent success. Such problems account for having to create hundreds, if not thousands, of actual embryos. Furthermore, even if an organism is born, it does not mean it was successful. In some of the actual cattle studies, when the clones were born, they were born with enlarged organs or malformed organs and eventually died subsequently a few days later.

Finally, the last disadvantage to animal cloning is that it is, through technology transfer, the means to achieve or move towards human cloning which is our next topic.

In human cloning, some studies have come out. For example, in 1993, Stillman and Hall performed studies where they did actual human embryo splitting. These researchers used abnormal embryos obtained from an IVF clinic. They got press. They were able to present this paper at a conference, but they could never publish their results, and they had to destroy all their results because they had bioethical conflicts when they were being reviewed at the University where they did the research.


5 See John A. Robertson, Procreative Liberty in the Era of Genomics, 29 AM. J. L. & MED. 439, 468 (2003) (noting that two hundred sheep embryos were created for every one successful pregnancy).


Also, Somatic Nuclear Transfer was achieved by Li Bo-yon of Kyunghee University in South Korea. This was announced in December of 1998. There have been some subsequent studies done since that one. This was done with a thirty-year-old woman, and I believe that the scientific research on the clone went either to the eight or the thirty-two cell stage. The researchers stated that they believed they could have implanted it into a woman if they wanted to.

The next issue for discussion is: “What makes a clone?” This can be better stated as: “What makes an individual?” One of the things we have to understand is the distinction between the two definitions of the word “clone.” There is, first, the actual biological definition of the word “clone,” and then there is the understanding of the general person on the street (or the Hollywood understanding) of the word “clone.” We have already discussed the first definition, the actual biological definition. But, the Hollywood understanding or person on the street would say that a clone is a complete copy of Tom Cruise, or Einstein, or Beethoven; furthermore, they would believe that that copy means that everything has been copied: the person’s body, the genetic make up, the intellect, the mind, the personality. Copying one’s personality is going to be far, far more difficult, I assure you.

The genetic copy is going to be also difficult to make. The individual is a composite of the following: genetics, which we refer to as nature, environment, which we refer to as nurture, and also, development. When we talk about nature, this means the genetic influences in the clone, in essence, from the donor cell. There are some limitations. When we have somatic nuclear transfer technique, it requires an egg, and the egg supplies an important constituent. It is an organelle, a structure called the mitochondria, which is the powerhouse of the cell providing ATP. However, that mitochondria also contains a small amount of genetic material, genes, loops of DNA, that actually code for certain proteins in the mitochondria. The only way you and I all get our mitochondria is from our mothers. Yep, we get it from the egg. We don’t get it from Dad, sorry, fathers.

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9 John Burton & Clive Cookson, Koreans Claim Human Clone Breakthrough, FIN. TIMES (U.K.), Dec. 17, 1998, at 8 (discussing Korean researchers’ announcement that they were able to cultivate or clone a human egg in its earliest stages).
But the reality is that if you were going to make a clone, the clone would not be one hundred percent, pure genetically identical if you use a foreign egg. The only way to achieve an absolute clone is to use the donor's nucleus, coming from the woman, and obtain an egg from that same woman. That is how to obtain a pure, one hundred percent genetic clone.

From the genetic aspect, also, clone DNA demonstrates gene damage from the donor. Dolly the sheep is one example of that. To go to “nurture” issues, remember that this is environmental influences - all of the influences on a person, such as the nutrition, the socialization, the education, et cetera. Did they have good books when you were growing up? Did they have their Flintstone vitamins when they were growing up?

But on top of that, another important factor that helps create the original individual is timing - the temporal factor. Take any great artist, any great creator, any great poet, and any person, and ponder what would have happened if they had been influenced at a different time of their life? Take Beethoven, for instance. What happens if he was given the piano or music lessons at a later time in life, instead of when he did? How would that have influenced his development with musical aptitude?

I give the best example of this to my students, and I use Arnold Schwarzenegger. Now, when I did this example, I was talking about 1998, before he became governor, obviously. But I say to my students, think about this. Arnold Schwarzenegger, Mr. Universe, body builder, action hero, actor: what if we clone him? But, instead we are not going to raise the Arnold clone in Austria where he will acquire his famed Viennese accent. We will raise him in Brooklyn, and we give him a Brooklyn accent. Moreover, we will not encourage the clone of Arnold to engage in any athletic activity, or any type of sports. As a matter of fact, we will sequester him and make him be a geek – a nerd. We are going to teach him how to hack into Microsoft. Oh, I cannot say that or it would be illegal! But we are going to teach the Arnold clone all the things very different from the original Arnold Schwarzenegger, and so, the result will be two different individuals here. First, Arnold Schwarzenegger, action hero, and now governor, and then this scrawny, thin kid who looks something like Arnold, but who is not big and muscular, and who
is kind of a geek and kind of nerd, and who does not have Arnold's Viennese accent. 

Let us move on to development. Development is the embryological and fetal development that occurs to an individual. These, in fact, are the uterine influences on a fetus. Now, researchers have even looked at clones, and found that the clones do not totally look one hundred percent identical to the donor. For example, the clones will have, in some animal cases, patches of fur that look differently colored. Researchers believe that that result was the influence in the uterus – development.

Some researchers have done mice studies, where they have a brood of mice in the uterus. The researchers have noticed that the neighboring male mouse fetus releases hormones that affect the actual brain development in the next female mouse fetus that is connected in the blood supply. Therefore, the uterus and the development in the uterus influence the development of this organism.

This raises the next question. What if we start experimenting and developing an artificial uterus? Will that have developmental effects on the clones? This involves bioethical challenges. To start, there was a paper that came out in 1998, wherein Dr. John Robertson advocated human cloning for the replacement of lost children.10 I submit to you that there is a problem there. The big problem is that parents that may have undergone incomplete grieving of their lost child. Hypothetical child "Johnny" dies, and understandably it is a very sad event. Under this theory, the parents could say, "Well, I've got some of the blood supply or tissue samples, let's make replacement Johnny."

Now, if that sounds so far-fetched and like a movie, remember, we have people now that actually have done this for the replacement of pets. We also have the psychological pressure placed by the parent on the clone to act as the original child. Now, no parent will probably sit there and say, "Yeah, I'm going to force the kid to be just like my former kid," but there is going to be that subtlety, overt or covert, conscious or unconscious,

especially as the child develops and looks more and more like the formerly deceased child. Finally, this reduces the personhood of the clone. In other words, the clone will know that it is a clone, or an entity that was born/created, not because its parents wanted you, but because you are serving a replacement purpose. Basically, the clone is replaced from the personhood and the individual sense, to serve a utilitarian purpose. The clone therefore serves but a single purpose.

Also, similarly, there lies another ethical conundrum. Dr. Neil First used cow eggs as donor eggs for cloning other animals. He was able to show that cow eggs may become the universal egg for all types of cloning experiments. He was able to use a cow donor egg to produce clones with rats, pigs, rabbits, and cows. He was able to do a lot of cloning. Now, this universal egg issue relates to the issue of the selling of human eggs in certain ads and on certain universities. I actually saw one advertisement on careerbuilder.com for a New York area hospital that was offering eight thousand dollars for a female to donate her eggs. Why pay eight thousand dollars when you can go down to the slaughterhouse, the abattoir, and get a whole mess of very viable eggs to do subsequent human cloning. Make no mistake: I am talking about the creation of human clones using a cow egg. The cost of cloning would be driven down.

The problem, here, though, is that clone will have cow mitochondrial DNA; that clone is going to have the mitochondria from the cow, not from a human. Therefore, if we talk in terms of percentage, that clone, although it might look human, would have some foreign DNA from another species. By the way, that DNA could be technically passed on to the human clone if it was a female, because females pass on their mitochondria to the next generation through their eggs. This would thereby pollute the human genome, and the human population with foreign DNA from a cow egg or any other universal donor egg. The ethical

11 See id. (noting that these "clones are interspecies since their oocyte come from a species other than the cow").
12 Id. (positing that Dr. First's "research suggests that the molecular machinery responsible for reprogramming the genome by the cytoplasm may be similar or identical in all mammals").
13 See generally Irene Sege, A $50,000 Dilemma on Campus: Top Students Wrestle With Egg Donor Lure, BOSTON GLOBE, Mar. 6, 1999, at A1 (discussing one couple's advertisement in college newspapers to buy embryos of a woman who met certain specifications).
question herein is, could the human clones be considered less than human as a result of these experiments?

Another issue is that there is a high risk of stillbirths and deformities with clone fetuses. A lot of the cloning experiments have not been tremendously successful with their rates of producing successful clones; in fact, they are certainly not with ten percent or greater success rates. As a matter of fact, the mice cloning studies had the best success rate with two point eight percent, and the sheep studies were certainly less than one percent. So I submit to you a question: Will defective humans be cared for, or will they be discarded? Will the less than perfect humans created from cloning be considered useful for nothing much more than risky experiments? Now, if that sounds rude or insulting, think about this: Hall and Stillman, when they did their human cloning experiments with embryos, used defective, abnormal embryos obtained from IVF clinics. Will we as a society consider clones defective or expendable, and therefore cheapen ourselves as we cheapen these lives of these individuals?

In the Roman Catholic tradition, stated in the encyclical In Donum Vitae, the instruction on the respect for life in its origin and on the dignity of procreation, replies to certain questions. They very clearly reject human cloning, stating that it is in violation of moral law, in opposition to the dignity of human procreation and of the conjugal union. In essence in part, they are saying that everybody has the right to live, everybody has the right to be a product of the joining of egg and sperm, and also to have a home that is the human uterus, right?

However, what about cloning for therapeutic versus reproductive reasons? Do we create clones and try to get some good out of it? This is the concept of proportionalism. We are going to create clones for the purpose of creating a supply of "spare parts" for other humans. The clone, in essence, is going to be the next generation of stem cells. Under this theory, the clone

14 Roberge, supra note 10 (listing poor success rates of animal cloning as a disadvantage of cloning).
15 Roberge, supra note 10 (summarizing success rates of various attempts at cloning in terms of live birth rate, and noting that Dolly the sheep was the 277th attempt by the Wilmut team to clone a sheep).
16 See generally Roberge, supra note 10 (noting that Stillman and Hall “used defective human embryos created using IVF methods, which were destined for disposal”).
17 See generally Roberge, supra note 10 (articulating need for Church involvement and leadership on human cloning so that our society does not create a “culture of death”).
does not have the right to live. The clone does not have the right to exist. We are just going to extract parts from the clone. If we fully accept this in society, how far are we, then, from taking apart much more developed organisms? In other words, are we far from going beyond just tearing apart a small ball of cells—perhaps going to full developed fetuses.

Moving on, there are many ways to bypass human cloning legislation. Right now, as one of my esteemed colleagues said earlier, we already have it. We, in the United States, do not have a legal ban on human cloning. All we said was that we would not use any federal dollars for human cloning research. That means no NIH and no NSF. So if I go to the Ford Foundation, the Rockefeller Foundation, or a whole host of other corporate suppliers, I can legally do human cloning in this country. And if that looks so bizarre, go to 1998 when Dr. Richard Seed was saying he was going to do his own human cloning. When confronted on CNN, he was asked what he would do, as far as research goes, if the United States made cloning of humans illegal. He said that I would not be a "big deal," because he would then just go to some country where human cloning was not illegal. Or, better yet, he could just do clandestine cloning in America. If you remember that myth of the Raelians with their claims of human clones—and I only say myth because there is no scientific data to back them up. They basically never told you where it occurred. They hinted here, there, everywhere else, but you can make a clandestine cloning facility. It does not take much. Or better yet, one other way to bypass the legislation is just declare clones not human.

21 Roberge, *supra* note 10 (describing Dr. Seed's articulated plan to clone himself with his wife's help).
Another means to approach this is to perform embryo splitting, which is far easier than nuclear transfer, and which is also easier to conduct at IVF clinics. As a matter of fact, there was some controversy in 1998 when some United States IVF clinics wanted to make more embryos for implantation. They wanted to split the embryos and follow what Stillman and Hall had done for their earlier work in 1993. But the IVF clinics were afraid to violate any human cloning bans. However, the reality is they could do this splitting of human embryos very easily, and legally. In some of the laws and some of the legislation I have seen in my web research, regarding the attempts to make human cloning for reproductive purposes illegal, only one phrase was used: somatic nuclear transfer.\(^{23}\) Such legislation never addressed embryo splitting.

Now, another way to bypass human cloning legislation would be very simple: artificial gestation. In other words, this involves artificial wombs. Basically, if legislation states that clones can be created but cannot be implanted into a woman, one could bypass the wording of the law by just having the clones raised in artificial wombs. Now that sounds like science fiction, or maybe something straight out of Aldous Huxley, with his *Brave New World*.\(^{24}\) In this slide, there is a picture of a goat fetus. Some of this work was done by Kuwabara, and also from Nobuya Unnos's work.\(^{25}\) These are researchers in Japan and in South Korea who are already working on development of an artificial placenta. This is a goat fetus after ten days of extra-uterine incubation. This shows that some attempts at this have already been performed.

One of the challenges that these studies faced was that the goat fetuses would sometimes start to stand up in the artificial

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\(^{24}\) See generally ALDOUS HUXLEY, BRAVE NEW WORLD, 1-6 (Perennial Ed. 1998) (describing future society in which people are bred in incubators rather than through natural birth, and person’s class in society depends on what programming they receive in incubation process).


\(^{26}\) See id. at 996 (affirming that their research was conducted at the University of Tokyo Department of Obstetrics and Gynecology in Japan).
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uterus. As an accident, the goat fetuses would pull out from their umbilicus the arterial/venous connections. Here is somewhat the schematic of their extra-uterine fetal incubation, EUFI system. To give you a perspective, when the animals tried to stand up, what the researchers had to do was paralyze them with certain neuroparalytic drugs. How were these animals “born,” as you might call it? The researchers would just remove them from the tub. But the animals had to be put on a respirator for awhile. And after they were finished with the respirator, the animal clones died within about an hour.

Remember when we talked about development? There is a lot of development that actually goes on inside of the womb. Think about it. Those of you that know someone who is pregnant will say. “I can feel the baby kicking.” A lot of these muscular contractions or other necessities of the uterus may be enhancements to muscular development. Pushing up against a resistance, that is, the uterine wall, etc. Without some of these resistances, even though you have developed the biochemical area and the oxygenation for an artificial uterus, there will be some inappropriate or missing development because the clone fetus will not have the same confinement, the same restrictions, the same pressure, touch, that occurs on the fetus in the uterus. But clearly this is an example of how this could influence development.

And furthermore, such artificial wombs could also be, I suggest to you and submit to you, used to bypass human cloning restrictions. It also could be used to culture clones and experiment on human clones. The one extreme example here would be to use human clones as test subjects to perfect our artificial placenta. After that we will be able to successfully use an artificial placenta in some cases of preventing miscarriage, etcetera, in normal humans. But, of course, these experiments would lead to further creation of defective clones.

So what is my conclusion? First, cloning is a technology that has arrived in society. Animal cloning has potential benefits. But the disadvantages must be clearly understood by both the public and the legislature. Human cloning is a technology that has arrived in society. The genie is out of the bottle. We are going to see this happen. How we control it and what we do is what the future is going to be, shall I say, shaping. Human
cloning has potential abuses; it contains many technical and moral challenges. The actual development of a true, pure human clone is next to impossible. If you think about it from an individual, making an exact carbon copy of an individual with intellect, mind, body, and soul is almost next to impossible. To make a pure genetic clone, it requires very select characters. Now, it is possible to create by embryo splitting that genetic copy. It is also possible in that extreme case to copy using a woman's self-donated egg and also self-donated nucleus, but aside of that, you will not get a complete copy. These factors have to be understood. Also, the human cloning regulations could be circumvented by a variety of legislative limitations and technical issues. Also, the failure to stop human cloning could result in clones being treated in some form of sub-human status, perhaps due to the reasoning of their development, the origin of their egg source, or the site of their gestational development. Finally, the rise of artificial placental technology may provide for another haven for human cloning technology and research. And with that I thank you very much. And I am open to comments.