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ARTICLE

Nuclear transfer to prevent mitochondrial DNA disorders: revisiting the debate on reproductive cloning

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Abstract Preclinical experiments are currently performed to examine the feasibility of several types of nuclear transfer to prevent mitochondrial DNA (mtDNA) disorders. Whereas the two most promising types of nuclear transfer to prevent mtDNA disorders, spindle transfer and pronuclear transfer, do not amount to reproductive cloning, one theoretical variant, blastomere transfer does. This seems the most challenging both technically and ethically. It is prohibited by many jurisdictions and also the scientific community seems to avoid it. Nevertheless, this paper examines the moral acceptability of blastomere transfer as a method to prevent mtDNA disorders. The reason for doing so is that most objections against reproductive cloning refer to reproductive adult cloning, while blastomere transfer would amount to reproductive embryo cloning. After clarifying this conceptual difference, this paper examines whether the main non-safety objections brought forward against reproductive cloning also apply in the context of blastomere transfer. The conclusion is that if this variant were to become safe and effective, dismissing it because it would involve reproductive cloning is unjustified. Nevertheless, as it may lead to more complex ethical appraisals than the other variants, researchers should initially focus on the development of the other types of nuclear transfer to prevent mtDNA disorders.

KEYWORDS: ethics, mitochondrial DNA disorders, nuclear transfer, reproductive cloning

Introduction

Mitochondrial DNA (mtDNA) disorders are usually severe disorders, caused by defects in energy production. Patients show a wide variety of symptoms, but generally the most energy-demanding tissues, such as the central nervous system, heart and skeletal muscles, liver and kidney, are affected. As there is no curative treatment, helping carriers of mtDNA mutations to have healthy children has been a central focus of attention (Taylor and Turnbull, 2005). One reproductive option to prevent the transmission of a mtDNA mutation from mother to child that is currently in preclinical

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development is nuclear transfer (or 'mitochondrial gene replacement'). In case of nuclear transfer to prevent mtDNA disorders, the mtDNA (which is located outside the nucleus, in the cytoplasm) is changed or replaced (Bredenoord et al., 2008a). This should result in healthy offspring with the nuclear genes of the parents, but without the mtDNA mutation (Gardner et al., 2007). Nuclear transfer can in theory be applied at different stages: before, during or after fertilization (de Wert, 2000; Brown et al., 2006; Roberts, 1999).

Germinal vesicle transfer

This would involve transfer of the germinal vesicle, removed from a recipient woman's immature oocyte, into an enucleated donor oocyte. Subsequently, the reconstructed oocyte will be matured and fertilized *in vitro* using a spermatozoon from the partner. The resulting embryo is then transferred to the prospective mother's womb.

Germinal vesicle transfer has not been applied clinically and is not considered to be one of the most promising types of nuclear transfer, particularly because its efficacy is doubted due to the poor developmental competence of in-vitro matured oocytes (Fulka et al., 2005; Taylor and Turnbull, 2005; Brown et al., 2006).

Spindle transfer

This would involve transfer of the chromosome–spindle complex, removed from a recipient woman's oocyte when the nucleus is undergoing the second division of meiosis, into an enucleated donor oocyte (Brown et al., 2006). Subsequently, the reconstructed oocyte will be fertilized using a spermatozoon from the partner. The resulting embryo is then transferred to the prospective mother's womb. As mature oocytes do not have a nuclear membrane, there was earlier scepticism about the safety of transfer at this stage (Brown et al., 2006). Recent studies, though, are promising. Tachibana et al. (2009) showed that spindle transfer is technically feasible in non-human primates: they transferred the chromosome–spindle complex of a mature oocyte to an enucleated donor oocyte, resulting in three thus-far healthy macaque infants, with minimal levels of carry-over of nuclear donor mtDNA.

Pronuclear transfer

This would involve transfer at the zygote stage (Brown et al., 2006; Craven et al., 2010). An oocyte of the prospective mother is fertilized using a spermatozoon from the partner, as well as a donated oocyte of a healthy woman (the oocytes have to be at the same stage). When the oocytes are 'half fertilized', the two pronuclei (distinct structures that become apparent after fertilization) are taken out of the donated zygote. Subsequently, the pronuclei of the intentional parents (containing their nuclear DNA) are transferred to the enucleated donor zygote. The resulting embryo is then transferred to the prospective mother's womb.

Studies suggest the safety and efficacy of pronuclear transfer in preventing the transmission of mutated mtDNA in a mouse model (Jenuth et al., 1996; Meirelles and Smith, 1997, 1998; Sato et al., 2005). A technical advantage is that during this stage the chromosomes are packed into the pronuclei, which would make it easier to collect and transfer them (Taylor and Turnbull, 2005). On the other hand, mitochondria surrounding the pronuclei may increase the amount of pathogenic mtDNA transplanted from the donor into the recipient zygote. Recent preclinical studies have shown that pronuclear transfer is feasible in human oocytes, resulting in embryos with minimal levels of carry-over of nuclear donor mtDNA (far below the threshold of disease expression) (Craven et al., 2010). A clinical application of pronuclear transfer has been reported once, resulting in a triplet pregnancy but no life birth (Zhang et al., 2003).

Blastomere transfer

The nuclear DNA of a donated oocyte from a healthy woman is removed. An oocyte of the prospective mother is fertilized using a spermatozoon from the partner. A blastomere of the resulting embryo is then transferred to the enucleated donor oocyte. Subsequently, the resulting embryo is transferred to the prospective mother's womb (Roberts, 1999).

Blastomere transfer has not been applied clinically. Some expect the success rate of nuclear transfer using a blastomere of an embryo to be much lower than nuclear transfer at the other stages, particularly because animal studies showed evidence of high heteroplasmy levels: the co-existence of mutant and normal mtDNA in an affected individual (Steinborn et al., 1998, 2000; Hiendleder et al., 1999; Ferreira et al., 2007). In addition, the resulting embryo may have a poor developmental competence (Roberts, 1999; Spikings et al., 2006), although higher rates of development are observed with embryonic-cell compared with somatic-cell nuclear transfer (Mitalipov et al., 2002). These technical impediments make whole blastomere transfer currently less suitable and promising than spindle or pronuclear transfer.

Although remaining technical and ethical difficulties need further attention, both spindle transfer and pronuclear transfer are promising future reproductive options for carriers of mtDNA mutations (Poulton et al., 2010; Poulton and Bredenoord, 2010). In addition, both these variants of nuclear transfer would not amount to reproductive cloning. On the contrary, blastomere transfer could. This type seems both technically and ethically the most challenging variant of nuclear transfer to prevent mtDNA disorders. The scientific community seems to avoid it, perhaps also in response to the fact that many jurisdictions have prohibited this variant because it may involve reproductive cloning. For example, when the Human Fertilisation and Embryology Authority (HFEA) had to decide on the research licence for experiments on pronuclear transfer, it explicitly mentioned that transfer of a nucleus of a cell of an embryo is prohibited (which, depending on the definition, could be perceived as reproductive cloning; see below) (HFEA summary decision RO153).

Notwithstanding the poor technical performance of blastomere transfer to prevent mtDNA disorders and its avoidance by scientists, this paper discusses the moral acceptability of blastomere transfer as a method to prevent

mtDNA disorders. The rationale for doing so is that it is worthwhile to have a conceptual and ethical discussion of this technique: most if not all moral objections that have been raised against reproductive cloning refer to reproductive adult cloning, while blastomere transfer would amount to reproductive embryo cloning (REC). Suppose that blastomere transfer turns out to be feasible and safe. The question then becomes whether researchers and regulatory authorities rightly exclude blastomere transfer as a possible reproductive option for carriers of mtDNA mutations with the argument that it may imply REC. If not, researchers should not feel impeded by this argument to consider and develop this option. This paper examines whether and to what extent the main objections brought forward against reproductive cloning also apply in the context of blastomere transfer. It will presuppose the safety of the relevant forms of reproductive cloning as a preliminary condition and focus on the objections of principle.

Reproductive (embryo) cloning

Strictly speaking, cloning means the production of a genetic copy. This paper refers to reproductive cloning as all applications of human cloning that result in the birth of a child genetically identical to an embryo or a born individual (Bredenoord et al., 2008a). In contrast to reproductive adult cloning, where the clone is a 'copy' of an individual made after his or her birth, the original cell in the application of nuclear transfer in question would be derived from an embryo. This would therefore be an instance of REC.

Whereas the types of nuclear transfer to prevent mtDNA disorders currently under development (spindle transfer and pronuclear transfer) do not involve REC, blastomere transfer could. It entails the transfer of the nucleus of a blastomere to an enucleated oocyte. This results in two identical embryos. If an 8-cell blastomere would be used, up to eight blastomere nuclei may be used to create identical embryos. If those embryos are subsequently transferred to the womb, this may result in the birth of children genetically identical both to the original embryo and to each other. Following the above definition of reproductive cloning, a child is still to be considered a clone if it is the only individual ever born as a result from copying the original embryo. Following a more narrow definition, this is not the case. According to this alternative definition of reproductive cloning, being a clone presupposes genetic identity with at least one other born individual. Whereas the first (broader) definition refers to the fact that a child is the result of genetic copying, the second looks at the consequence of the procedure: the birth of genetically identical individuals. According to the latter definition, whether blastomere transfer implies REC depends on (i) the number of embryos transferred and (ii) whether this leads to a pregnancy and live birth of at least two (identical) children. If only one cloned embryo is transferred to the womb and the embryo does not split, this will not result in the birth of genetically identical children. If, however, more embryos are transferred, this may result in the birth of several clones.

Do moral objections against reproductive cloning also apply to blastomere transfer in the context of mtDNA-disease?

As it is clear that blastomere transfer may indeed amount to reproductive cloning, the moral significance of this conceptual conclusion needs to be addressed. This section will briefly discuss the main moral objections that are brought against reproductive cloning. The question to be answered is whether those objections amount to valid moral arguments against nuclear transfer aimed at preventing the transmission of mtDNA disease.

'It is repugnant and unnatural'

A first objection against reproductive cloning is that it would be repugnant. According to Kass (2002), repugnance may be the expression of wisdom, beyond reason's power to articulate why something would be wrong. If, and insofar as, Kass means that emotional reactions should not directly be dismissed as they may point to important considerations that otherwise may be overlooked, then the current paper agrees. However, the second step should always be to subject these emotions to rational analysis, because otherwise it would imply a permit for moral prejudice (Nussbaum, 2004). The critical scrutiny of arguments is precisely necessary to prevent ethics to get bogged down in gut feelings. After all, moral feelings may be misleading and send one in the wrong direction. For example, some people may have strong moral feelings about homosexuality or about the inferiority of some sections of the population. Ethical reflection and analysis may teach convincing arguments are needed to hold and defend such a position (Gillon, 1999).

An adjacent variant of this objection is that reproductive cloning would be unnatural or artificial. There has been an extensive debate on this so-called argument of nature, with the dominant conclusion that it is fallacious. In the context of reproductive cloning, Fukuyama (2002), for example, has deployed this argument. He calls for an absolute prohibition of reproductive cloning because it involves a highly unnatural form of reproduction. This seems rather thin as a counterargument, requiring further explanation of why unnaturalness would be morally problematic or relevant. Unnaturalness as such cannot be a valid argument — if it were taken seriously, humans should stop practicing medicine (and many other activities).

The proponents of these objections will probably also regard reproductive cloning in the context of mtDNA disease to be repugnant and unnatural — Kass (2002), for example, calls for an absolute prohibition of all types of reproductive cloning, REC included. For the reasons outlined above, these objections are not held to be decisive neither in general, nor in the context of mtDNA disease.

'We are creatures, not creators'

The second possible objection expresses feelings of uneasiness regarding human intervention in the creation and shaping of future persons. This type of argument rests on the

notion that 'we are creatures, not creators' (Cole-Turner, 2003, p. 195). The transformation of human procreation into manufacture, of begetting into making, would be problematic (President's Council, 2002). For Sandel (2007), genetic engineering is objectionable because it expresses a stance of mastery and dominance to the world: 'Genetic engineering to create designer babies is the ultimate expression of the hubris that marks the loss of reverence for life as a gift'.

Hubris is a well-known theme in Greek tragedy, in which the main actor, by challenging the gods or their laws, is inevitably heading to his downfall. Similarly, by denouncing genetic engineering (reproductive cloning included) as a type of hubris, the objection is that these are acts of excessive pride or arrogance that are likely to lead to nothing good. This objection is not valid for two reasons.

First, the validity of the view depends on a contestable normative anthropology. An anthropology that contends that people should not explore the limits of their knowledge and capacities, and that seems to summon people to know their place. If one does not share this specific portrayal of mankind, this argument is not convincing. Contrarily, this paper would rather encourage people to explore new technology and new paths for curing disease rather than invoke distrust of technology.

Second, insofar as this objection asserts that reverence for life as a gift would eventually would be lost, it may actually be interpreted as a slippery slope argument. The question is whether the dreaded position at the end of the slope indeed would be morally unacceptable. Would it be problematic that people would not perceive life as a gift? And does seeing life as a gift automatically imply that one should not alter it, or that one should not reproduce in alternative ways? If there would be a slippery slope here, the first steps have been set long ago, with the introduction of assisted reproduction treatment, which could be perceived as the first steps 'from chance to choice'. It is difficult to see why reproductive cloning would be morally much different from other artificial reproductive technologies used to prevent genetic disease.

'It is a violation of human dignity'

A third line of objections against reproductive cloning holds that it violates human dignity. Dignity is a much contested and vague concept and no agreement on the meaning of the term exists (President's Council, 2008; van der Graaf and van Delden, 2009). It is mostly used to indicate that human beings have intrinsic moral worth, but this forces one to specify what gives human beings this intrinsic worth (Kass, 2008). Since human dignity comes in such competing versions, it is understandable that authors have dismissed the concept as useless or vague (Beyleveld and Brownsword, 2001; van der Graaf and van Delden, 2009). The current paper will nevertheless try to scrutinize this objection by using two opposed conceptions as formulated by Beyleveld and Brownsword (2001): human dignity as empowerment or as constraint. These two conceptions make clear that human dignity can be deployed both in support of autonomy and as a constraint on autonomy (Beyleveld and Brownsword, 2001).

The first conception, human dignity as empowerment, is particularly used in the post-Second World War international treaties on human rights. The intrinsic dignity of human beings is the foundational idea, the justification for the recognition of human rights (Beyleveld and Brownsword, 2001). As Caulfield and Brownsword (2006, p. 72) have put it: 'In this reading, human dignity is an engine of individual empowerment, reinforcing individual autonomy and the right to self-determination'. Insofar as human dignity is equated with the capacity for autonomous action, this understanding of human dignity will be discussed in the next section, when autonomy and the right to an open future are addressed.

The concept of human dignity is also and increasingly used as a justification for condemning practices such as reproductive cloning. Recent international treaties have used human dignity in this way. The Council of Europe for example states that the deliberate creation of genetically identical human beings (i.e. reproductive cloning) is contrary to human dignity (CoE, 1998). The United Nations Universal Declaration on the Human Genome and Human Rights states that 'practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted' (UNESCO 1997, art. 11; United Nations, 2005). Those treaties deploy human dignity as an argument to reject reproductive cloning, but they do not further explicate how human dignity is to be understood or what its foundations are. It is, important that these treaties further underpin why and how they use human dignity, in order to enable a moral dialogue.

'It is a violation of the child's right to an open future'

A fourth line of objections is that reproductive cloning would violate — what Feinberg (1980) in another context coined — the child's right to an open future. Although debate is possible about the interpretation of this concept, taking it as a negative anticipatory autonomy right would be the most relevant and appropriate in our discussion. This means a right to have one's future options kept open until one is capable of making one's own decisions.

The strong version of this argument counsels that a child's right to an open future may be violated in the sense that the clone has to live in the shadow of its 'original'. The child's right to ignorance about its future would be violated, as the clone, being genetically identical to someone else, knows too much about itself (Jonas, 1974). The strong version, however, is untenable: it rests on too strong an account of genetic determinism. Genetic identity does not equal personal identity (Gillon, 1999). The clones would not be identical persons, as personality and character are not determined by genetics alone, but by a complex interaction of social, environmental and indeed genetic factors (British Medical Association, 1999; Buchanan et al., 2000; de Wert, 2000). Currently, existing monozygotic twins show a broad range of similarities and dissimilarities, thus demonstrating that sharing identical genotype and environment does not result in identical persons (Harris, 1997). The weaker version, however, should be taken more seriously. This version of the argument counsels that the child's right

to an open future may be violated as the child has the feeling that it knows too much about itself (Holm, 1998).

It is useful to emphasize here that this argument is primarily developed in the context of reproductive adult cloning. What about its validity in the context of REC? This argument would in any case not hold true in two situations regarding REC. The first exception would be when only one child is born. Following the more narrow definition of reproductive cloning, the child is not to be regarded as a clone in the first place, which means that the question whether cloning would affect the child's open future does not even arise. Although in terms of the broader definition the resulting child would indeed be a clone, this has no implications for the moral acceptability of blastomere transfer, as the child will not have to live with another 'co-clone'. Being alone as a clone, the child will not have to suffer from living in the shadow of a genetically identical individual. The second exception is when the twins, conceived by means of REC, are born simultaneously; this would not be different from identical twins in the natural course of events (which can be considered as naturally occurring clones; British Medical Association, 1999). Although they start their lives as genetically identical twins, and although they may share many characteristics, they also begin their biography at the same time. They will thus be ignorant of the future choices of the other (Buchanan et al., 2000).

Delayed twins

The main ethical bottleneck regarding REC concerns the possible asynchrony between two (or more) cloned children. What if, out of one single blastocyst, different embryos would be made, cryopreserved for future use and transferred later? This could result in a 'delayed twin' (British Medical Association, 1999): a clone with a (much) older twin-brother or -sister (or several identical siblings). This may indeed affect the sense of freedom of the delayed twin. The delayed twin may experience psychological distress by growing up in the shadow of an older sibling. After all, as the clones will grow up in the same family, they will share not only identical DNA but also a similar environment. If the delayed twin is transferred shortly after its older sibling, they may differ only 1 or 2 years in age. The delayed twin may (wrongly) think that the choices and the course of life of its older twin is an inevitable path. Or perhaps the parents may have this perception. It is not thought that a clone's right to an open future is violated merely because he or she or his/her surroundings believe that a clone's future is already determined, given that this belief is based on an erroneous genetic determinism (Brock, 2002). Nevertheless, the clone may still experience psychological stress.

The first question, then, is whether the delayed twin(s) would have an acceptable quality of life. One could argue here, following Parfit (1984), that as long as a child/clone does not have a life so awful that it would be better off dead, bringing it into existence will not harm the child. This is because the alternative for this child would have been non-existence (this child could only be born as a clone). Insofar as violating the interests of the future child is concerned, this line of reasoning is generally accepted. There is, however, less consensus about whether this settles the issue with regard to justifying assisted reproduction. Although no harm may be done in the sense of a violation of the child's interests, this does not make it a matter of moral indifference what quality of life the child can be expected to have (Arras, 1990; Steinbock and McClamrock, 1994; Parker, 2005; Glover, 2006; Bredenoord et al., 2008b). It is still meaningful to say in a more general sense that bringing a child into the world that will seriously suffer is to cause avoidable harm. The reasonable welfare standard, which was defended earlier as the best way to take into account the welfare of the child, allows assisted reproduction treatment (reproductive cloning and nuclear transfer included) insofar as there is 'no high risk of serious harm' for the resulting child (de Wert, 1998; Pennings, 1999; Bredenoord et al., 2008b). This standard entails the view that for treatment to be justified, the child to be must have a reasonable chance of an acceptable quality of life.

The question is whether the delayed twin would be at high risk of serious psychosocial harm. Clearly, no hard evidence exists. Nevertheless, it is doubted whether the delayed twin will psychologically suffer to such an extent that this provides a contraindication in light of the reasonable welfare standard. Whether the twins differ 1 year or 20 years in age may also influence the psychological wellbeing of the delayed twin, but also this is speculative. Some have brought forward the view that the delayed twin may even have an advantage, because he or she may learn from the older twin (Brock, 1998). In any case, to conclude that reproductive cloning would result in a high risk of serious psychological harm for the child is premature. Nevertheless, if people in the daily surroundings of the clones would treat them as copies or negatively approach them, then psychosocial harm would become a self-fulfilling prophecy. Not merely because the younger twin would feel restricted by the older brother or sister, but because it would feel restricted by the expectations and (negative) feelings in his/her surroundings. So, this objection may become true if it is allowed to be true.

In summary, this paper does not see overriding grounds to reject blastomere transfer to prevent mtDNA disorders beforehand, even when a delayed twin would be brought into the world. However, it remains impossible to know the precise psychosocial consequences for the resulting children. Would it therefore be better to avoid the creation of delayed twins as much as reasonably possible? This could be achieved by transferring several cloned embryos simultaneously or by starting a new (stimulation/nuclear transfer) cycle if a couple wishes to have another child.

Avoiding delayed twins by multiple embryo transfer

If several cloned embryos are transferred simultaneously, the resulting children will start their lives simultaneously. For reasons outlined above, it would seem that this will not lead to psychological harm (for it is similar to naturally occurring monozygotic twins). Transferring all blastomeres of the embryo may in theory result in up to eight children. What about the transfer of two, three or four embryos? The dilemma would then be as follows. Transferring several cloned embryos simultaneously may on the one hand avoid possible psychological problems, but on the other hand

seriously increase medical complications (for the twins as well as the mother) and parental stress (and this may in turn cause stress in the children) (Braude, 2007). Furthermore, data indicate that the quality of life of children born after assisted reproduction treatment is higher if they are born one at a time (Fauser et al., 2005). With regard to regular IVF, a strong consensus exists that, because of the health risks of multiple pregnancies, no more than two embryos should be transferred — and the current tendency in IVF is even heading towards single embryo transfer (Braude, 2007).

Whereas the psychological risks for delayed twins are speculative, the psychological and health risks in the context of multiple pregnancies are known to be substantial. When balancing these, it is preferable to avoid the known and substantial risks and to transfer only one or maximally two cloned embryos simultaneously.

Avoiding delayed twins by starting a new cycle

Choosing to transfer only one or two cloned embryos leads to the question what should be done with the remaining blastomeres or cloned embryos. One option would be to cryopreserve all cloned embryos. The question, of course, is whether cryopreservation of these reconstructed embryos would be feasible (the cryopreservation of biopsied embryos, for example, has not been very successful so far), but suppose it would be. The primary reason for doing this would be to avoid having to start a new stimulation/nuclear transfer cycle if after unsuccessful transfer the couple would want a further try. But what if the procedure was successful and 2 years later the parents return with the request to help them expand their family? One option may then be to thaw and transfer one of the cryopreserved embryos. The other option would be to start a new stimulation/nuclear transfer cycle. The dilemma here is whether avoiding delayed twins compensates for the efforts, costs and risks of starting a new stimulation/nuclear transfer cycle. When deciding about this, the known risks and burdens of ovarian stimulation have to be balanced with the speculative psychological risks for the delayed twins. As no further data regarding nuclear transfer are at hand, this appraisal cannot be done at this moment. It is currently sufficient to conclude that, although the fact that blastomere transfer involves reproductive cloning is not considered to be a decisive objection, it may in practice lead to complex ethical considerations. Other things equal, this constitutes an argument that supports the current focus on the development of the other types of nuclear transfer. In addition, those describing absolute or high moral value to embryos will only accept germinal vesicle transfer and spindle transfer, as these are the only variants of nuclear transfer that would not involve the destruction of a zygote or embryo — although the further development of these techniques in the preclinical stage will probably involve the creation and destruction of embryos for research (Bredenoord et al., 2008a).

Conclusion

This paper has discussed the moral acceptability of reproductive cloning in the context of blastomere transfer to prevent mtDNA disorders. More specifically, it has discussed the acceptability of REC. It is concluded that there are no arguments that render REC morally unjustified beforehand. If blastomere transfer results in the birth of one child, then (other things equal) this type of nuclear transfer is ethically comparable to nuclear transfer using oocytes or zygotes. The simultaneous birth of two (cloned) twins should not be considered morally unjustified either. Although bringing into existence a delayed twin raises concerns about a child having to grow up in the shadow of an older clone, it remains speculative whether this would lead to psychosocial harm. The argument would therefore not amount to a decisive objection against blastomere transfer. On the other hand, the fact that the relevant concern is not completely implausible either does provide, other things equal, a reason to focus at least initially on the further development of spindle transfer and pronuclear transfer. After all, blastomere transfer may in clinical practice lead to a complex appraisal of the relative weight of avoiding delayed twins versus avoiding a multiple pregnancy or the burden of starting a new stimulation/nuclear transfer cycle.

The fact that a specific version of nuclear transfer with the aim of preventing the transmission of mtDNA disease would possibly involve reproductive cloning cannot convincingly be construed as a categorical moral objection against the possible use of this version of the technology. Of course, the overall acceptability of using nuclear transfer for this purpose would also depend on the safety and efficacy of the procedure.

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