The Ethics of Mitochondrial DNA Replacement Techniques: The Morality of Three Parent Babies and the Non-Identity Problem

I. Mitochondrial Replacement and Its Purpose

In 2015, England became the first country to legalize so-called “three-parent babies,” or fetuses created by combining the genetic material of three different individuals. The technique in question, mitochondrial replacement, is designed to give a potential offspring healthy mitochondria from a donor in order to avoid passing inheritable mitochondrial diseases (which are always passed maternally, since a fetus inherits its mother’s mitochondria) from a mother to her offspring. Many have questioned the ethics of using the technique, citing concerns that mitochondrial replacement is a eugenics issue that will lead to the creation of designer babies, or that the technique runs afoul of the non-identity problem. I will argue that there are no

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1 I am deeply grateful to S. Matthew Liao, Regina Rini, Duncan Purves, Andrew Mark Erickson, the New York University Bioethics Department, and the audience at the Bowling Green State University Conference on the Ethics of Emerging Technologies for their comments. I am especially grateful to Liao and Purves, whose discussions helped me properly formulate my view and arguments before writing the paper itself.

2 While I can appreciate why someone would call them “three-parent babies,” given the fact that the resulting children would technically possess genetic material from three different parents, I do not believe the term is truly accurate. In later sections of this paper, I argue that mitochondria should more accurately be considered symbiotic organisms that developed into eukaryotic organelles. Changing them out is much more akin to organ transplants, which we normally do not think affects personhood in any way. Additionally, it seems that the biological “parents” are those that contribute the necessary chromosomes to form a human zygote. Since the mitochondrial donor does not do this, I do not believe it is correct to say that the resulting offspring have three parents. The issue can be complicated depending on which technique is used: if we are not simply swapping out mitochondria (which is not yet possible), but are rather moving genetic material from place to place, the child also inherits the other organelles of the donor parent. However, since the organelles themselves do not possess genetic material (aside from the mitochondria, of course), I believe we can ignore the issue. The child would also temporarily inherit some RNA left over from the original DNA in the cell, but any new RNA produced would stem from the new genetic material, so this can be ignored as well.
eugenics concerns present in the current application of the technique, and that the non-
identity problem does not arise given a DNA-based view of personal identity.

Mitochondrial diseases make life extremely difficult, if not impossible, for those
afflicted with them: “Mitochondrial dysfunction has been recognized as a significant
cause of a number of serious [multi-organ] diseases. Tissues with a high metabolic
demand, such as brain, heart, muscle, and central nervous system, are often affected.”.
Further, “symptoms may include deafness, blindness, diabetes, muscle weakness, and
heart, kidney, and liver failure.”. These symptoms pose significant obstacles to living a
long, enjoyable life. Mitochondrial replacement offers a solution by enabling doctors to
give the potential fetus new mitochondria, avoiding the disorders entirely. Medical
procedures that parents choose for their offspring are considered morally permissible if
they provide a clear medical benefit to the patient in question, and since this is clearly
the case with mitochondrial replacement techniques, it seems that this version of three-
parent babies is morally permissible.

How exactly does mitochondrial replacement occur? At present, there are two
viable techniques. The first, called pronuclear transfer technique, involves fertilizing two
separate eggs, one with the intended parents’ genetic material, the other with donor
genetic material. The respective nuclei are then removed, and the donor zygote is
injected with the intended parents’ DNA, resulting in a zygote without mitochondrial
disorders. Unfortunately, this technique is not as effective as one would hope, as
Craven et al.\(^1\) were not able to achieve great results: “Of the reconstructed Embryos,

\(^1\) Amato, Tachibana, Sparman, and Mitalipov, “Three-parent in vitro fertilization: gene replacement for
the prevention of inherited mitochondrial diseases,” Fertility and Sterility, Volume 101, Issue 1 (January
\(^\text{iBd.}\)
\(^1\) Craven, Tuppen, Giggains, Harbottle, Murphy, Cree, et al., “Pronuclear transfer in human embryos to
8.3% developed to the blastocysts stage.”. However, it is significant to note that their study used abnormally fertilized eggs donated from IVF treatments, eggs that contained three pronuclei. Abnormally fertilized eggs are significantly hampered in their developmental capacities, so it is possible that normally fertilized eggs would be much more viable.

Alternatively, Amato et al. propose spindle transfer technique, which “uses micromanipulation techniques to transfer the genetic material (the spindle with maternally derived chromosomes attached) from one unfertilized oocyte to another from which its own nuclear material has been removed. This reconstituted oocyte is then fertilized to allow embryo development.”

II. Potential Objections

The most popular objection to modified IVF treatments like mitochondrial replacement and other genetic alterations involves speculation over the development of “designer babies,” babies that are genetically engineered to have specific traits by altering the genetic material of the parents. As with most new techniques, we are presented with worries over violating “the natural order,” but also with potentially disadvantaging low-income individuals who could not afford the procedure (or simply refused the technique on other grounds): poor individuals and those who declined the treatment would not be capable of paying to set their children up for success the same way rich individuals could, perpetuating and even worsening the difference between

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1 Amato et al. (2014).
3 Ibid.
classes. One popular film, *Gattaca* (1997), even speculated that a new class of genetically-enhanced elite would be formed altogether, capable of controlling every other class, resulting in discrimination based on genetic code that leads to economic oppression. However, the objection presents no significant problem because the technology merely affects mitochondrial DNA, which has no known bearing on any genetic traits outside of the mitochondria themselves. In addition, the host egg (in the case of donated eggs) or replacement mitochondria (in the case of donated mitochondria) are selected anonymously from the donor pool, so there is no potential for parents to purposely select donors with favorable traits. A future child may wonder who his or her third “parent” is, but this is no different than any other case in which donated genetic material has been used. Thus, no eugenics issues arise because the technique merely eliminates the damaging disorders, and because there is no potential for selecting one’s donor in the first place: even if there were some other benefits one would gain from the donor’s mitochondria, one could not purposely acquire them. The resultant offspring would be subject to the genetic lottery just as much as any other fetus, except that one type of terrible disease has been removed.

Another objection to mitochondrial transfer is that we may not know the specific impacts the process itself will have on the patient in the future. It is possible that the technique itself might cause future mutations that could destroy the quality of the patient’s life, and even lead to premature death. However, I will ignore this possibility for two reasons. First, preliminary testing has not indicated any such side effects. Second, this worry is present with virtually any new technology. Obviously, if we discovered devastating side effects, the technique would be prohibited; however, if we

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were to rule that the technique was morally prohibited by other principles \textit{anyway}, prohibiting it based on side effects would be redundant. We must first answer whether or not the technique is ethical in principle before we enter into consequentialist calculations.

A more general objection to mitochondrial replacement can be made: as in the case of any incidence of germline modification or IVF, there are always questions about whether or not it is permissible to create and destroy human embryos. In this case, the worry is over what happens to the genetic material removed from the destination oocyte in pronuclear and spindle transfer techniques. However, the ethics of using human embryos as a whole is far too complicated to treat in one paper. If we were to rule that the whole field was unethical, the natural extension would be that mitochondrial replacement was unethical as well. I shall take it as a given in this paper that such research \textit{is} permitted for the sake of evaluating whether or not this specific use of embryos is permitted.

The most significant challenge to mitochondrial transfer involves the non-identity problem, which concerns the notion that we may be bringing different people into the world than we would have if we did nothing differently. Proposed by Derek Parfit in 1984\textsuperscript{10}, the non-identity problem states that certain acts cannot be said to benefit or harm any individual person because the very nature of the act necessarily creates a different person. For example, a pregnant girl cannot truly be said to harm her child by refusing to wait until she is older to procreate because if she chooses to wait a different sperm will fertilize a different egg, creating a completely different child.\textsuperscript{11} Conversely, we cannot make people better off by refraining from actions like depleting our natural

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resources because such actions determine which people will come to exist: if we behave differently, different people will be born. The actions are a necessary condition of those individuals’ existences, and so changing our actions cannot make them any better or worse off, but merely remove them from existence.

There seems to be an implicit principle in medicine, especially in regard to procedures that one chooses for one’s child or for another individual, that any medical procedure must have a clear physical or psychological benefit to the patient, otherwise there is no reason to choose it at all. If a couple had a baby in the conventional way, and the mother possessed a mitochondrial disorder, the disorder would be passed on and the baby would have a significantly lower quality of life. If, on the other hand, we used mitochondrial replacement, then the resulting baby would have a much better, perhaps even longer, life. But if we use mitochondrial replacement, is it possible we are creating different babies? And if we are creating two different babies, we couldn’t possibly say that the technique benefited the child who would have had a mitochondrial disorder because that child would no longer exist. In order to answer this worry, we

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* Parfit, 361-364.

13 Notice that this leaves a fair bit of wiggle room. There are many cosmetic procedures that could be considered as “medical” insofar as they consist of surgeries of some sort. For example, while a face-lift may not constitute a physical benefit in terms of curing a specific disease, it may give one enough of a psychological benefit to render it a beneficial procedure to the patient. What the principle of beneficence in medicine wouldn’t allow is a procedure that gives no benefit of any sort whatsoever.

14 One significant worry some commenters have expressed is that the non-identity problem presents no ethical issue at all in this case. If one accepts Parfit’s “No Difference” view, one can admit that a new person is created but believe that this fact does not matter, i.e. it holds no ethical weight. I believe the non-identity problem does present an ethical worry despite the No Difference view for two reasons. First, if the central criterion for choosing a medical procedure involves benefiting someone, then there is a procedural issue in simply creating a new person, since one has not satisfied the criteria necessary to begin the procedure at all. Second, supposing we at least adopt a flexible view of moral status, it is at least possible that a person or being with moral status was created during the initial IVF treatment to obtain the parent DNA in pronuclear transfer. If this is the case, then it is at least possible that by carrying out the procedure, we destroy one being with moral status or, if you prefer stronger language, we “kill one possible person.” I use “at least possible” to avoid strong commitments toward viewing fetuses, embryos, or zygotes as people or as mere collections of cells in order to apply my argument to both camps. When we are unsure of moral status, it seems intuitive to air on the side of caution. Given these considerations, the non-identity presents a strong ethical consideration that must be addressed.
need to determine what constitutes personal identity, and thus whether or not the non-identity problem is relevant.

III. Genetics and the Supervenience of Personal Identity on Biological Identity

Pinning down what constitutes personal identity is a difficult matter, and much ink has been spilled in attempting to boil it down to a specific property. Perhaps the best candidate in biological terms is the set of genetic codes one possesses. Indeed, when one needs to identify whose cell a given cell is, one would test the DNA of the cell to determine a match. This seems to match the intuition that all of the cells with my DNA are mine, specifically because they possess my DNA: the DNA itself constitutes personal identity. DNA is also continuous throughout one’s life: while the specific base pairs and molecules are surely different with each replication, these pairs take the same form in subsequent replications unless a mutation occurs. One might argue that different genes are activated in different types of cells, but this is analogous to turning lights on in a house: the house (DNA) has the capacity to demonstrate certain characteristics (being lit or not), and what determines whether or not these characteristics are activated involves turning a switch on or off (activating a gene or not activating a gene). In both cases, the property determining the characteristic is still there (DNA for an organism, the electrical wiring in the walls for the house).

* Mutations present a significant worry, but since mutations do not tend to occur and then somehow manifest themselves in every cell of the body, I do not believe they present an issue in practice. Additionally, I know of no mutation that affects the generation of consciousness or other rational capacities traditionally associated with personhood, so it does not seem that there are any mutations that currently affect personal identity.
DNA also plays a significant, if not the dominant, role in determining the form of the cells that house it. Skin cells look and behave very differently than brain cells, and what determines how the cells develop is the genetic code present in them. In essence, the genetic code is responsible for the development of the matter around it, and thus the organism itself. Many have argued that personal identity arises from one’s consciousness, a psychological state generated by the specific activities of the brain. On such an account, what goes on in the brain, and how the brain develops, is essential to determining personal identity. Since the genetic code in each brain cell is responsible for the development and the activities of the brain matter, which gives rise to consciousness, the set of genetic codes one possesses seems fundamental in determining personal identity, as it plays a crucial role in dictating the activities of the matter to which many of us attribute identity.

It may be unclear, however, how we make the jump from genetic codes to personal identity, or how we make the jump from identity in single cells to the complex notion of identity manifested in multicellular organisms. The answer lies in the supervenience of personal identity and consciousness on what we should call “biological identity” and the material that composes it. Consciousness, insofar as it is a psychological property that arises out of our brain matter and its activities, supervenes on the brain matter itself: we cannot have a change in consciousness without some change in the brain matter itself. Further, we cannot have any fundamental changes in the brain matter itself without changing the genetic material that dictates its form; only accidental changes, changes that do not affect the fundamental characteristics of that

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*I include “activities” to capture the sense that what proteins are produced in cells derives from the genes activated in each cell’s DNA. This in turn controls the activities of the cells. Consciousness seems to be a result of the activity of our brain cells, so, by transitivity, consciousness is the result of our DNA. I do not claim to understand the full relationship, but only that consciousness supervenes on DNA and its activities.*
matter, are possible. Now, one might object to this point by pointing to the phenomenon known as neuroplasticity, or “the plasticity of the brain matter.” Brain matter does not remain static throughout the life of the organism: it develops and changes over time, without changes in the nature and structure of DNA, most notably from its developmental level during infancy to its maturity in adulthood. This presents a significant complication. Empirically, the brain matter does change throughout our lives, without radical changes in genetic material, but we do not usually claim that numeric and personal identity shift with those changes, so it seems that my genetic view is false. However, I emphasized “fundamental changes” with an eye toward these developments: the constancy I wish to capture is the fact that our genetic material remains the same in terms of the overall pattern and personal markers. Additionally, the changes captured by neuroplasticity are, in a sense, normal: they occur as a natural part of biological development as the brain organizes for more complicated tasks and different biological functions. So while some developmental changes do occur, they are not the kind of changes that produce new people. Further, the presence of these developmental changes despite the consistency of genetic material does not challenge the supervenience relation because those changes are normal, and occur as a direct result of the genetic coding (since the brain matter changes to fulfill the structure set forth from the DNA). To challenge supervenience, we would need to show that changes in genes presumed to affect the brain matter do not produce changes at all, or that developmental changes in the brain matter itself were not controlled by genetic material. It is crucial to note that I am concerned with the form the brain matter takes and the capacities that are produced, and changes of that kind would occur if certain genes were changed, as cells with different properties that would give rise to different capacities would be produced during each replication.
On the micro scale, genetic material is certainly responsible for the biological identity of the cell, as the material is the feature by which we determine whose cell a cell is. Since this material permeates throughout the body, and thus gives rise to the body’s other features by influencing development of features like consciousness, which gives rise to personal identity on many accounts, personal identity supervenes on biological identity. Thus the biological identity of the cell is instrumental in determining whether or not a new person has been created. Once an egg (a specific type of cell configured such as to develop into a full person when in possession of a full set of DNA) is fertilized with the genetic material of the male’s sperm, it possesses the full, new set of DNA required to develop into a person, and this separates it from its parents’ identities.

IV. The Non-Identity Problem Does Not Arise

If we use the set of genetic codes one possesses as the bases of personal identity, it seems that mitochondrial replacement is morally permissible because it does not create a different person, but rather improves the quality of life of the person created. At present, there are three formulations of the technique:

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Talk of a genetic account suggests a potential problem: if identity is based on genetics, what should we make of genetically identical twins? I do not claim that genetic identity is the only factor in determining personal identity. Part of the reason I do not entirely reject the Organism view is that it suggests many useful factors in determining the continuation of personal identity and of differentiating between organisms that might actually share the same genetic code. The fact that DNA gives rise to regulatory capacities in two separate places that develop independently of each other suggests that one may still have a genetic account of personal identity in general without being committed to counterintuitive conclusions. I claim merely that the genetic code is the fundamental property that remains constant over time that constitutes one individual’s identity. If we have two individuals, we will have two different persons with identity over time.
(1) Switching the fertilized nucleus from the affected egg cell into a donor egg cell.

(2) Taking the genetic material from the sperm and the mother’s egg and fertilizing them in the host egg cell.

(3) Replacing the mitochondria in the egg cell.

In scenario (1), pronuclear transfer technique, the mother’s egg cell is fertilized with the father’s DNA, creating the set of genetic codes that will be responsible for the development of the child. The material is then transferred to a “healthy” enucleated donor cell that has mitochondria free of genetic disorders. Since the genetic code is what constitutes the biological identity of the cell, a different person has not been created because the fundamental property of identity has simply been switched to a new location, with healthier tools to work with.¹

In scenario (2), spindle transfer technique, the genetic material that will guide the development of the person is fertilized in the donor cell itself. In this case, no non-identity problem could arise because there was no person yet at all. We are not affecting whether or not a certain person still exists after a certain procedure meant to improve the quality of that person’s life because no person exists until the procedure is completed (you cannot have a person without a complete set of DNA). Spindle transfer

¹ We might draw another argument from this talk of “moving the location” of the genetic material, and thus the person-generating property. S. Matthew Liao has argued that moral status results from the presence of the genetic material, whatever that might be, that gives rise to the properties that make up moral agency. This suggests a further argument: since we have not created a new set of codes that convey moral agency, and thus moral status, but merely moved them from one site to another, we have not created a new or different person. See S. Matthew Liao, “The Basis of Human Moral Status,” Journal of Moral Philosophy 7 (2010) 159-179.
technique seems preferable to pronuclear transfer because one does not have to worry that we are potentially destroying one possible person: in order to do pronuclear transfer, an egg must first be fertilized, and then its genetic material removed to make way for the parental DNA. But if we are linking biological and personal identity to possessing a full set of genetic codes that would spark full organismic development, we might be creating two people in the process and destroying one. Spindle transfer does not create this worry, so it is preferable to pronuclear transfer. Pronuclear transfer may still be permissible based on one’s entire conception of how we use embryos, which, as I said, is a question for another paper. I will merely say that spindle transfer is preferable because it avoids such worries entirely.

Scenario (3) would be the most ideal situation, as I fail to see how it could cause an identity issue on most accounts of personal identity. In (3), one would merely swap out the defective mitochondria for healthy mitochondria; this is analogous to giving someone a kidney transplant, which we do not normally consider a personal identity issue. Unfortunately, this technique is not currently a viable option. In one version of the technique, one would remove the defective mitochondria and then inject healthy ones. This has proven difficult, as the cell generally dies before the new mitochondria can be installed. In the other formulation of the technique, healthy mitochondria are injected into the cell. It is impossible to specifically remove the defective ones based on our current technology, so the result is merely a moderate benefit.19

V. An Alternative Account: The Organism View And The Non-Identity Problem

19 If one reaches different conclusions about personal identity, and thus retains concerns over the non-identity problem, this technique would still remain viable. One would moderately benefit the resulting child without creating a different person.
An Alternative view we might consider is the Organism view of personal identity endorsed by S. Matthew Liao\(^a\) and others.\(^a\) The Organism view holds that what constitutes an organism, with its own personal identity, is the capacity to regulate certain “life processes,” such as metabolism, replication, and movement. These capacities, sustained over a lifetime, present the continuity many identity theorists search for.\(^a\) According to Liao, the Organism view holds that something (X) is an organism (with personal identity) if:

a) X begins to exist when the capacity to regulate and coordinate its metabolic and other life processes is there; b) X persists as long as there is what may be called ‘organismic continuity,’ which is the continuing ability to regulate and coordinate its metabolic and other life processes; and c) X ceases to exist when the capacity to regulate and coordinate its metabolic and other life processes is permanently gone.\(^a\)

On Liao’s view, moving the genetic material of the zygote from one cell to another would create a different organism, because the original host (the cell that was fertilized) would permanently lose its capacity for life, metabolism, and replication, and


\(^a\) Liao attributes the view collectively to Snowdon (1991), Carter (1982), and Quinn (1984).

\(^a\) Because every atom of our bodies is replaced at some point or another, many philosophers argue that there may be no such thing as identity-through-time, as nothing remains constant during one’s entire lifetime. Some writers have argued that consciousness fits the bill, but consciousness is subject to drastic alterations, and we lose consciousness when we sleep, suggesting the continuity sought after doesn’t exist. Looking for continuity in the form of regulatory capacities provides a potential solution, as these are fairly constant, and we do not need to be actively exercising a capacity in order to possess one.

\(^a\) Liao, 2009, 6.
the capacities of the destination cell would be permanently transformed. This means that scenario (1) runs afoul of the non-identity problem on the Organism view.

However, a closer inspection of my account and the Organism view suggests that these worries are unfounded. The thrust of the Organism view’s argument is that an organism arises, and can be defined by, the continuity of its capacities. The elegance of such a view is that it avoids the problem of trying to find something that remains constant throughout the organism’s lifetime. While this may not ever occur in terms of the material constituents of the organism, it seems that DNA itself, at least in terms of the form it takes in replications, is constant throughout one’s life, and since the DNA itself is what gives rise to the regulatory capacities of cells, it seems that these capacities are not interrupted in situation (1). The DNA may be transferred from one cell to another, but the capacities themselves remain constant, and simply manifest themselves in different material than in the original cell. The point on display is that the capacities themselves have not been permanently destroyed, as is the criterion for organismic death, but merely have been relocated to occur in a different cell. While the individual organelles in the original cell may lose their ability to function without DNA to direct them, this simply implies that those parts have died: the parts that die only have their regulatory capacities insofar as DNA has the capacity to direct them. This is analogous to the fact that one’s gallbladder will cease to function when a brain is no longer present to regulate the person’s metabolic systems. Thus in situation (1), the non-identity problem does not arise because the capacities of the fundamental regulatory property of the cell, and the organism as a whole, do not lose their functionality. Further, even though replications of the cell’s DNA spawn genetic material composed of different molecules, the capacities of the material are never interrupted, suggesting that DNA is the fundamental property that remains continuous throughout our lives.
Many philosophers might suspect that my DNA-based view of biological and personal identity is in deep disagreement with the Organism view. In fact, the opposite is true: I strongly agree that the continuity of capacities across the life of an organism is essential to determining that organism’s identity. However, I simply believe we can trace the origins of those capacities to the existence and activities of the genetic material itself, which does present us with a fundamental property that holds constant throughout the life of organisms that possess it.

One final objection can be made on behalf of Organism theorists who do not accept my DNA-based view, as well as philosophers who do accept the view. In all three formulations of mitochondrial transfer technique, the mitochondria themselves are different by the end of the process than the ones present at the outset. This may be troubling in virtue of the fact that mitochondria possess their own DNA, and thus on my account would create separate capacities. In (1), this is because the genetic material is moved to a cell with new, healthy mitochondria: in (2), the regulatory capacities first arise in a cell with different mitochondria than would otherwise have been present; and in (3), new mitochondria are added to the cell to pick up the slack for defective mitochondria. However, this does not present a significant worry. Mitochondria, while classified as organelles of the host cell, may more properly be thought of as symbiotic organisms that live inside our cells, based on the notion that mitochondria were originally separate organisms that symbiotically developed to live inside eukaryotic cells, and since they have their own DNA, and thus a change in mitochondria would not constitute a change in a person’s genetic code. The mitochondrial activity of producing ATP by itself is not enough to sustain the life of an entire cell; it takes the capacities of the host cell’s genetic material to coordinate the other organelles into utilizing that energy properly to keep a cell, and thus an organism alive. Thus the
specific material generating mitochondrial activity is not what matters in determining the organismic continuity of cells and organisms.

VI. Conclusion

In this paper I have argued that “three-parent babies” created using mitochondrial transfer are an ethical product of IVF technology because they drastically improve the quality of life for the patient. If we were in fact creating different people by tinkering with the mitochondria of the zygote or by moving the genetic material from the original egg cell to that of a donor, this would not be possible, as we could not have improved the patient’s quality of life: we would in fact have created a numerically different person, and there would have been no condition to improve in the first place. However, if we consider the role DNA plays in giving rise to an organism’s capacities, and the fact that the form of the genetic material remains continuous throughout one’s lifetime, creating continuous regulatory capacities, no such worry presents itself: since the DNA remains intact when it is moved, the capacities are not permanently destroyed, nor is the material that generates them. However, we should be cautious in choosing which technique to employ, as pronuclear transfer would involve the creation and destruction of a second person on a DNA based account. Spindle transfer technique avoids this problem by waiting to create any zygotes until the maternal DNA is in the donor egg. Thus mitochondrial replacement is morally permissible, with spindle transfer as the preferable mode of operation.