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CHRISTIAN INFLUENCE IN A SECULAR WORLD

GM babies with 3 or 4 parents

Maternal Spindle Transfer and Pronuclear Transfer: An Ethical Discussion

Calum MacKellar

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Contents

Foreword

Government ministers are planning to allow scientists to create genetically modified (GM) babies. In 2014 Parliament is expected to vote on allowing the creation of three-parent (or even four-parent) children in cases involving mitochondrial disease.

If the UK decides to allow the practice, Britain will become the only country in the world to formally legalise GM babies, whose genetic changes will be passed on to future generations.

Christians will want to show love and compassion to parents who have medical disorders which can be passed on to their children. We must love our neighbour (Mark 12:31). Yet the Bible also clearly teaches the sanctity of human life. Every human being is made in the image of God and life is sacred from conception (Genesis 1:27, 9:6; Psalm 51:5). The Ten Commandments uphold the sanctity of life and show that humans have two parents, a father and a mother (Exodus 20:12-13).

We are very grateful to Dr Calum MacKellar for this incisive report, which clearly explains the dangers of the proposals and key ethical objections. A helpful glossary can be found on page 26.

The proposals are strongly backed by leading members of the scientific establishment. The Human Fertilisation and Embryology

Authority is recommending the move, but its 2012 public consultation found that over half of respondents opposed changing the law, and the safety fears remain.

Although this involves complex science, at its heart the issue is about the sanctity of human life – whether it will be protected today and for future generations of parents and children. It should therefore concern us all.

Humphrey Dobson
Deputy Director (Policy and Staffing)
The Christian Institute

Introduction

The desire by parents to have children 'of their own', or at least as much as possible 'of their own', is the driving force behind the popularity (and financial success) of fertility clinics throughout the world.[1]

In addressing the issues raised by the regulation of assisted reproduction, it is very important therefore to examine the deep bonds that exist between parents and their offspring. For example, many parents, as the responsible partners for bringing a child into existence, know intuitively that they belong to the child and that the child, in receiving life, belongs to them, i.e. there exists a sort of mutual belonging.

The deep sense of loss or incompleteness felt by many parents unable to be directly responsible for bringing their child into existence is one of the underlying reasons for them to seek assisted reproduction. In other words, the fact that prospective parents even consider, let alone undergo, expensive procedures for artificial reproduction indicates the importance they attach to the biology of creation.

In this context, a lot of hope has recently been expressed that new research could eventually be useful in preventing some forms of inherited mitochondrial diseases which may be fatal in offspring. Mitochondria are very small entities found in all the cells of the human body and constitute 15 to 35 per cent of a cell's total mass. Depending

on its function, a cell may contain a few hundred to several thousand mitochondria. They are considered to be the power source of the cells, giving them the energy to survive. But for a cell to function and replicate properly, the 37 genes in every mitochondria must interact properly with the 20,000-30,000 genes in its chromosomes.

Individuals only inherit their mitochondria from their mother since they are already present in the egg when it is fertilised by the sperm cell. Thus they are inherited in a very different manner to the genes in the chromosomes which are inherited equally from both father and mother.

Mitochondrial disorders arise when genetic mutations in the mitochondria or in the chromosomes limit the energy supply in the cell. In the UK, recent studies indicate that while one in 200 children are born with a potentially dysfunctional mitochondrial mutation, about nine persons out of 100,000 have mutated mitochondria that could give rise to a mitochondrial disease including muscle weakness, neurological problems, issues with sight and/or hearing, kidney disease, diabetes or heart disease. On average, only one child in 6500 is affected by a serious mitochondrial disease which may, in some instances, lead to death in infancy.[2]

Procedures

The new treatment being proposed consists of two possible procedures called Maternal Spindle Transfer and Pronuclear Transfer. These may enable a woman to have a child that she may consider to be 'her own' and who is free from some forms of mitochondrial disorders even though her eggs are affected by serious mitochondrial dysfunction.[3]

Maternal Spindle Transfer

The procedure (see diagram on page 12) involves the following stages:

- Eggs from the woman wanting a child, but who is affected by dysfunctional mitochondria, are removed from her ovaries.
- The small spindle shaped entity containing the chromosomes (and most of the genes) in the unfertilised egg is then removed and the remaining emptied egg discarded.
- The egg of a second woman, who has donated her eggs containing healthy mitochondria, is then taken and its own spindle (containing all the chromosomes) removed and discarded.
- The spindle from the first woman is then transferred to this emptied egg of the second woman.

- Once this new egg is obtained it is then fertilised by the sperm of the first woman's partner to form an embryo.
- This embryo is finally transferred back into the uterus of the first woman wanting the child with the hope that it may give rise to a child without any mitochondrial disorders.

Maternal Spindle Transfer would give rise to a child generated, from a biological perspective, from three different individuals (a chromosomal mother, an egg mother and a sperm father).

Pronuclear Transfer

The procedure (see diagram on page 13) involves the following stages:

- Eggs from the woman wanting a child, but who is affected by dysfunctional mitochondria, are removed from her ovaries.
- One of these eggs is fertilised with the sperm of her partner. Once this happens all the chromosomes (and most of the genes) of the egg are regrouped into the female pronucleus and all the chromosomes of the sperm are regrouped into the male pronucleus.
- These pronuclei are then removed and the remaining fertilised egg (with the dysfunctional mitochondria) discarded.
- An egg of a second woman, who has donated her eggs containing healthy mitochondria, is then taken and fertilised with the sperm of a man who has donated his sperm.
- The pronuclei of this second fertilised egg are then removed and discarded.
- Once this has taken place, the pronuclei of the first couple (who want to have the child) are then transferred into the emptied fertilised egg of the second couple.

- The fertilised egg from the second couple containing the chromosomes (and most of the genes) from the first couple is then left to develop and transferred back into the uterus of the first woman wanting the child with the hope that it may give rise to a child without any mitochondrial disorders.

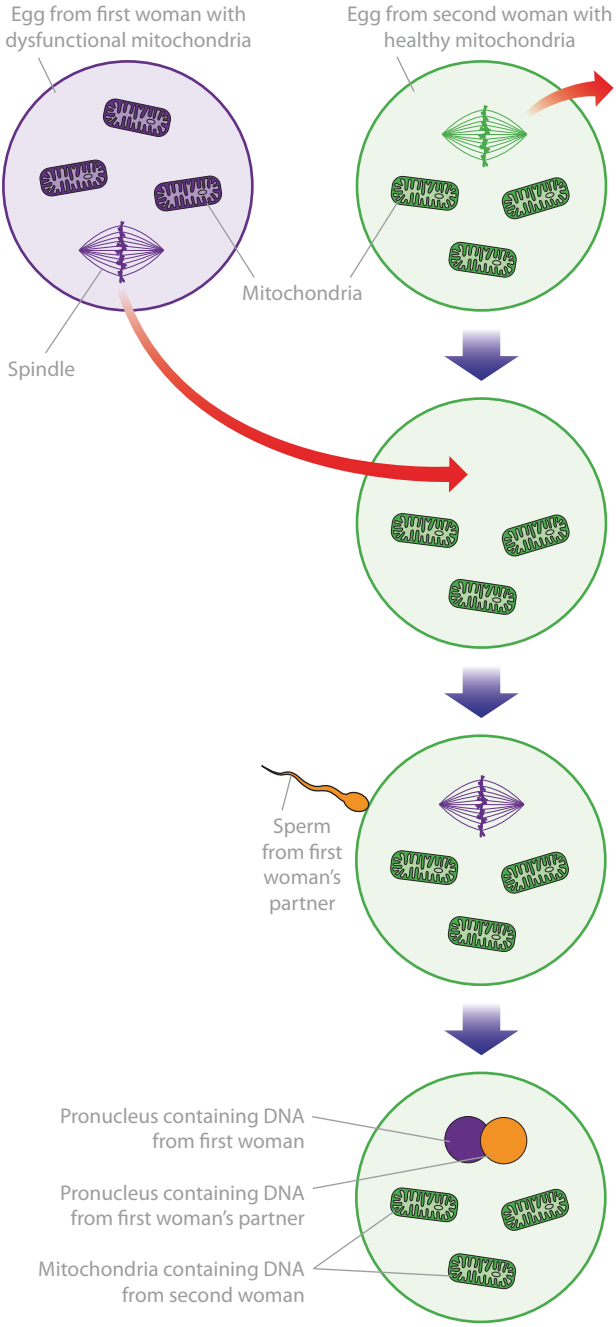
Pronuclear Transfer would give rise to a child generated, from a biological perspective, from four different individuals (a chromosomal mother, a chromosomal father, an egg mother and a sperm father).

Note:

With both Maternal Spindle Transfer and Pronuclear Transfer, a transfer of chromosomes is taking place from an unfertilised or fertilised egg to another unfertilised or fertilised egg respectively. It is, therefore, not so much a process of 'mitochondrial donation' or 'mitochondrial transfer' but of 'chromosomal transplantation'.

The Human Fertilisation and Embryology Act 2008 permits the UK Government to bring forward regulations to allow the creation of three and four parent children where there is a problem with mitochondrial disease.[4] These regulations must be voted on in both Houses of Parliament. The regulations could permit both the Maternal Spindle Transfer and Pronuclear Transfer methods.

Maternal Spindle Transfer



The spindle from the second woman's egg is removed and discarded.

The spindle from the first woman's egg is transferred to the emptied egg of the second woman.

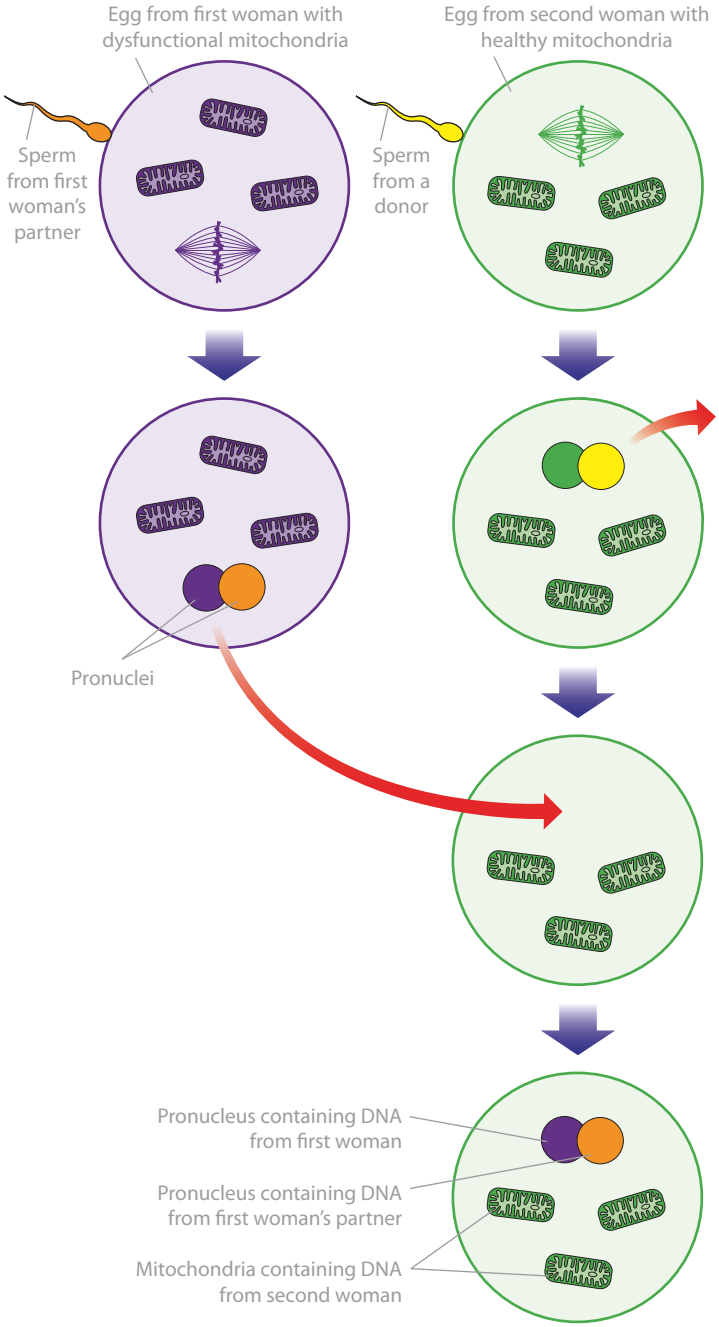
The emptied first woman's egg is then discarded.

The new egg is fertilised by the sperm of the first woman's partner.

An embryo is formed through the involvement of three biological parents.

The embryo is then transferred into the uterus of the first woman.

Pronuclear Transfer



The first woman's egg is fertilised with sperm from her partner to form an embryo.

The second woman's egg is fertilised with sperm from a donor to form a second embryo.

In each embryo the chromosomes from the egg and sperm regroup into a set of pronuclei.

The pronuclei from the second woman's embryo are removed and discarded.

The pronuclei from the first woman's embryo are transferred into the emptied embryo of the second woman.

The emptied first woman's embryo is then discarded.

A new embryo is formed through the involvement of four biological parents.

The embryo is then transferred into the uterus of the first woman.

Ethical discussion

As with most new developments relating to embryology, a number of important ethical issues arise with these new procedures which need to be examined before they are ever considered in clinical applications. These include, first of all, a number of biomedical challenges that must be addressed relating to the safety and efficacy of the procedure.

1. Biomedical risks

Biological risks for the prospective child

Both Maternal Spindle Transfer and Pronuclear Transfer are relatively novel procedures and would require many stringent checks before they can be considered as safe and effective for clinical use.[5] Because they are somewhat similar to the cloning procedure with which serious unresolved biological problems remain, it is to be expected that both these new procedures will face similar challenges.[6] As a result of the risks and uncertainty involved, the Human Fertilisation and Embryology Authority (the UK's regulator in this area) recommended in 2011 that children born from Maternal Spindle Transfer or Pronuclear Transfer should be monitored for a very long period of time (probably many years) after birth.[7] Proponents have no way of predicting what the long-term consequences might be.

Risks to women

It should also be noted that many more donated eggs would be necessary for both these procedures to become possible. However, the egg retrieval process for the women giving the eggs in assisted reproduction is not risk-free since ovarian hyperstimulation may take place following aggressive hormonal treatments.[8] Around 5 per cent of In Vitro Fertilisation cycles cause moderate or severe symptoms which may result in disabling strokes or even, in very rare circumstances, the death of the woman.[9]

2. Similarity with reproductive cloning

Maternal Spindle Transfer and Pronuclear Transfer are both somewhat similar to Somatic Cell Nuclear Transfer technique (SCNT) which is commonly known as cloning. This technique was made famous through the birth of Dolly the sheep in 1996.

With SCNT the eggs from a woman are removed from her ovaries and one of these eggs is taken and its spindle (containing all the chromosomes) removed and discarded. Once this is done, the nucleus (containing the full set of chromosomes from the father and mother of an individual) is removed from a somatic cell (i.e. a cell other than sperm or egg cells or their precursors) of the person to be cloned. This nucleus is then transferred to the emptied egg and stimulated in order to enable cell division and so become a developing embryo. The obtained embryo is finally transferred back into the uterus of a woman with the hope that it may give rise to a child with the same chromosomal genes as the person to be cloned.

If Maternal Spindle Transfer and Pronuclear Transfer were to be accepted, since they are similar to SCNT, it would make it more likely that the reproductive cloning of persons who already exist is eventually accepted. For example, in the case of a woman with

mitochondrial disease. It is unavoidable that any practical support for these procedures would facilitate the development of reproductive cloning that most people and governments (including in the UK) do not wish to see become a reality.

3. Similarity with the 'male-egg' proposal

Interestingly, when Maternal Spindle Transfer was first discussed a number of years ago, it was suggested that the procedure could eventually help homosexual men have children 'of their own'. The speculation was that the chromosomes of a sperm cell, instead of an egg cell, could be transferred into another emptied egg thus creating a 'male-egg' which could, subsequently, be fertilised by the sperm of another man to become an embryo. This would then be implanted into a surrogate mother for gestation. Of course, this proposal would need to address many significant biological problems, including the fact that both sets of chromosomes would come from men.[10] But again, any development in Maternal Spindle Transfer is certain to give practical support to this possibility.

4. Moral status of the research embryo

For Christians who seek to protect human life as soon as it is created, a significant ethical question arises since human embryos are destroyed during this procedure.[11]

In this regard, the UK Human Fertilisation and Embryology Act 2008 defines an embryo in Section 1 (2) as:

> *"an egg that is in the process of fertilisation or is undergoing any other process capable of resulting in an embryo."*

Generating embryos for research would contravene international law

For Maternal Spindle Transfer and Pronuclear Transfer to be accepted for clinical use, it is unavoidable that many human embryos will be created solely for research purposes which will, eventually, be destroyed. This creates a serious ethical problem since these human embryos can be considered as having the same moral status as adult human persons who are then killed for the benefit of others.

Moreover, such a proposal would contravene international law since the Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine (ETS – No. 164, Entered into force on 1 December 1999) indicates that:[12]

> *Article 18: The creation of human embryos for research purposes is prohibited.*

In this regard, the Explanatory Report for Article 18 mentions that:

> *116. The article does not take a stand on the admissibility of the principle of research on in vitro embryos. However, paragraph 2 of the Article prohibits the creation of human embryos with the aim to carry out research on them.*

At present, out of the 47 countries of the Council of Europe only **two member states** (the United Kingdom and Belgium) have publicly indicated that they have no intention, at present, of signing or ratifying this convention. This is because, amongst other things, it would prohibit the creation of human embryos for research through cloning or other procedures (which the UK has already legalised) so that experiments can take place on them for up to 14 days after their creation.

Pronuclear Transfer would require the destruction of embryos even for routine treatment

UK law defines an embryo as "an egg that is in the process of fertilisation". Therefore, if Pronuclear Transfer were to be accepted as a form of routine treatment, the procedure would require under UK law that two embryos are destroyed each time to reconstruct a third embryo with new healthy mitochondria. This would be seen as deeply offensive and unacceptable to Christians who believe that life begins at the moment of creation of the embryo.

5. Modifying the human genetic heritage of descendants

Because parents would be intervening, with intent, into the genome (i.e. the complete set of genes, including chromosomal and mitochondrial genes) of their children in Maternal Spindle Transfer and Pronuclear Transfer the procedures could be considered as germ-line gene interventions.[13] This means that genetic modifications may be passed on to a child and all subsequent descendants.

It would be the first time such intentional genetic modifications of descendants are considered and would open the door to further genetic alterations of human beings with unforeseeable consequences.

Because of this, intentional germ-line interventions are prohibited under international law. Thus, if the UK were to allow both these procedures, it would create a very serious precedent, resulting in grave risks for the future.

The prohibition on intervening in the human genome of a person before he or she is born is reflected in the two following legal instruments:

(A) The United Nations Education, Scientific and Cultural Organization (UNESCO) - Universal Declaration on the Human Genome and Human Rights (Adopted on 11 November 1997) indicates in Article 24 that germ-line interventions could be considered as a practice that would be "contrary to human dignity".

(B) The Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with Regard To The Application of Biology and Medicine indicates that:[14]

> *Article 13: Interventions on the human genome*
>
> *An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.*

In this regard, the Explanatory Report for Article 13 mentions that:

> *91. Interventions seeking to introduce any modification in the genome of any descendants are prohibited. Consequently, in particular genetic modifications of spermatozoa or ova for fertilisation are not allowed. Medical research aiming to introduce genetic modifications in spermatozoa or ova which are not for procreation is only permissible if carried out in vitro with the approval of the appropriate ethical or regulatory body.*
>
> *92. On the other hand the article does not rule out interventions for a somatic purpose which might have unwanted side-effects on the germ cell line. Such may be the case, for example, for certain treatments of cancer by radiotherapy or chemotherapy, which may affect the reproductive system of the person undergoing the treatment.*

6. The procedures represent eugenic practices

Since the genome of future children is being intentionally modified through Maternal Spindle Transfer and Pronuclear Transfer, both these procedures could be considered as eugenic practices. These are defined as strategies or decisions aimed at affecting, in a manner which is considered to be positive, the genetic heritage of a child, a community or humanity in general.[15] As such they would contravene Article 3 of the Charter of Fundamental Rights of the European Union (Proclaimed in Nice on 7 December 2000) which indicates that: "In the fields of medicine and biology ... the prohibition of eugenic practices, in particular those aiming at the selection of persons" must be respected.[16]

7. Kinship issues

Perhaps one of the most fundamental questions arising from the use of Maternal Spindle Transfer and Pronuclear Transfer is the fact that more than two individuals are participating in the generation of human life. From this perspective, although chromosomes are extremely important in the bringing into existence of a child, it is impossible to just reduce the concept of parenthood to the persons who contributed chromosomes. This is because without an emptied egg or fertilised egg from another couple, no new life would ever have existed. Indeed, from an ethical perspective, chromosomes by themselves have no real value. They only become ethically meaningful if they are transferred into an emptied egg or fertilised egg and left to develop.

In this regard, all those participating in the process of bringing a child into existence may be considered, in some form and to varying degrees, as his or her parents. They may then also experience some or all the corresponding aspects of parenthood bonds and mutual belonging which arise between parents and their children.

Thus, in the case of Maternal Spindle Transfer and Pronuclear Transfer, it is the amount of individual participation in the creative

process that may be crucial to the existence of parent-child bonds. This means that the provision of an emptied egg by a donor woman or an emptied fertilised egg by a donor couple can in no way be seen as insignificant.

With natural reproduction, the 'real' parents and the chromosomal providers are the two same persons, but with Maternal Spindle Transfer and Pronuclear Transfer the identity of the 'real' parents becomes very complex and may vary quite considerably. In other words, a genuine risk exists that future children may be deeply confused and distressed in their understanding of who their parents really are. This may have serious repercussions on the manner in which they define their identity and self-understanding.[17]

In addition, it may be the case that parents who use dubious forms of assisted reproduction may be bringing a child into existence for their own sakes without fully considering the best interests of the future child. Though the social or chromosomal parents may concede to tell their child the truth about his or her conception when he or she is older, they would then have to understand that the child may wish to see and know his or her sperm or egg donor parent(s). This is because the child may want to express a sort of 'love' or affection which he or she may already experience internally.

8. Sperm and eggs represent the whole person

Procreation is never something that happens in a virtual world or in a complete vacuum. It takes place through the participation of the man and the woman as whole persons including their body and soul. More specifically, this participation takes place through the means of reproductive cells (sperm and egg cells). In this regard it is important to consider how these reproductive cells can be understood from a Christian perspective in the context of reproduction. This is not an easy matter but, generally, each reproductive cell may be considered as a kind of representative of each of the partners in the procreative

process. As such, each sperm cell becomes a representative of the whole man and each egg cell becomes a representative of the whole woman.

When parents procreate in a normal way they also give of themselves in love wholly and unconditionally in the sense that it is not only a portion of the person that takes part in the procreation. It is the whole person that takes part, with his or her whole body and soul. In other words, when a parent participates in the act of procreation they give themselves to, and accept, the other parent totally, completely and unconditionally in their entire existence. The procreators do not withhold anything from themselves.

This means that when sperm and egg cells participate in the bringing into existence of a new person, they express the complete fusion of the whole persons, the parents, from whom they were produced. The sperm and egg cells can then be considered as 'ambassadors' in the same way that a political ambassador represents, in his or her person, the whole of a country.

Moreover, it should be recognised that the unreserved acceptance between the parents with all their gifts and limitations should also 'expand' onto the child. This means that when partners in a couple accept each other for 'better or for worse' including all their biological disorders, they should unconditionally accept any child resulting from their relationship. This includes all the child's potential disorders, since he or she is brought into existence by the unconditional acceptance of the parents' sperm and egg cells which represent them. The possibility, therefore, of parents selecting or choosing the kind of child they would like to have (a kind of eugenics) would mean that they would no longer unconditionally accept each other since they would no longer accept the reproductive cells representing each other's wholeness.

Of course, sperm and egg cells have no moral value of their own but when they come together to form an embryo, their representative wholeness cannot in any way be dismissed as unimportant. On the

contrary, it is fundamental since it is the reproductive cells that are the means for procreating another specific 'whole' living child.

This also means that if the sperm and egg cells were significantly modified in a technical manner, such as with Maternal Spindle Transfer, the question must be asked whether they would still represent the wholeness of the partners from whom they originated. Would they not be seen, instead, as being foreign in the same way as if the reproductive cells of a foreign man or woman (i.e. from outside the couple) were used? The procreative process may then be taking place with reproductive cells that no longer represent the partners and could be seen as an intrusion into the exclusive relationship of the couple. This is an exclusiveness which also extends into the reproductive relationship of the couple.

Conclusion

Based on the ethical arguments relating to:

(1) the biological risk to the potential child and mother, and to future generations,

(2) the disregard for the moral status of the human embryo,

(3) the undermining of the sense of identity of the future child, and

(4) the intrusion of third or fourth parties into the reproductive exclusivity of a couple,

Maternal Spindle Transfer and Pronuclear Transfer cannot be considered by Christians as morally acceptable. Moreover, it should be noted that new alternatives for the treatment of mitochondrial disorders are already being pursued by scientists. These alternatives can be considered as far less controversial (such as seeking to repair faulty mitochondria)[18] and should be examined and developed instead of considering Maternal Spindle Transfer and Pronuclear Transfer.

Glossary

Chromosome: an organised structure containing the genetic material found in the nucleus of a cell. A normal non-reproductive human cell contains 46 chromosomes, 23 coming from the father and 23 coming from the mother.

Germ-line Intervention: a procedure that may pass on genetic modifications to descendants.

Maternal Spindle in an egg: a structure in an egg made up of microtubules that include the chromosomes.

Mitochondria: very small entities found in all the cells of the human body considered to be the power source of the cells giving them the energy to survive.

Nucleus: a small membrane-enclosed body found in human cells which contain all the chromosomes.

Pronucleus (plural: **Pronuclei**): the nucleus of a sperm cell or an egg cell during the process of fertilisation, after the sperm cell enters the egg cell and prior to their fusion. Sperm and egg cells generally only have 23 chromosomes, in other words, only half the number of chromosomes of a non-reproductive human cell.

References

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[11] Ling, J, *When does human life begin?* The Christian Institute, Newcastle, 2011, pages 41-42

[12] This is a legally binding document when ratified by a country. So far, 29 Member States have ratified this Convention with another 5 signing their intention to ratify. The UK has not signed or ratified this Convention.

[13] *Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review*, Nuffield Council on Bioethics, London, 2012, page 58

[14] This is a legally binding document when ratified by a country. So far, 29 Member States have ratified this Convention with another 5 signing their intention to ratify. The UK has not signed or ratified this Convention.

[15] See for example, *Telegraph.co.uk*, 20 January 2012, see http://blogs.telegraph.co.uk/news/cristinaodone/100131389/the-three-parent-family-this-is-another-attempt-to-dehumanisedisabled-people/ as at 14 November 2012

[16] The Charter of Fundamental Rights of the European Union (27 Member States) is not a treaty, constitutional, or legal document, and has the ambiguous value of a 'solemn proclamation'. However the EU institutions (and other institutions such as the European Court of Justice) are not going to contradict the Charter since they have 'solemnly proclaimed' it.

[17] *Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review*, Nuffield Council on Bioethics, London, 2012, pages 52-57

[18] *e! Science News*, 13 March 2012, see http://esciencenews.com/articles/2012/03/13/correcting.human.mitochondrial.mutations, as at 14 November 2012

GM babies with 3 or 4 parents

Maternal Spindle Transfer and Pronuclear Transfer: An Ethical Discussion

Should scientists be allowed to create genetically modified children who have three – or even four – parents? The Government wants to let scientists go ahead.

The UK would become the only country in the world to legalise GM babies. Although the aim is to help parents with medical disorders, this issue raises grave ethical concerns. What would be the psychological effects on a child when they learn they have three (or four) parents? Who can predict the consequences of altering the human germ-line with genetic changes passed on to future generations? Is it safe?

In this insightful and cutting-edge report, Professor Calum MacKellar explains the new procedures and discusses the many ethical issues raised.

Dr Calum MacKellar is a Visiting Professor in Bioethics with St Mary's University College in Twickenham, London. He has worked with the Bioethics Division of the Council of Europe in Strasbourg and written widely on bioethical issues.

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