Mitochondrial donation or the reality of the myth of 'three parents, one baby'

Introduction

In February 2015, MP's debated a motion in the House of Commons to approve the *Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015*. Having passed that hurdle, the Regulations still require approval by the House of Lords before coming into force on the anticipated date of 29th October 2015. The objective of the Regulations is to permit the use of new assisted reproductive techniques which will avoid the transmission of serious mitochondrial disease.

What is mitochondrial disease?

Mitochondrial disease passes from mother to baby and can result in serious debilitating conditions from which there is no cure. Mitochondrial disease can be inherited from the mitochondrial DNA, from the nuclear DNA or from a spontaneous mutation of the DNA and can present itself by way of mental, physical or developmental abnormalities either at birth or later in life. By way of example, Sharon Bernardi lost seven children; six babies and her son aged 21 to Leigh's disease, a progressive mitochondrial disease affecting the central nervous system,[1] this illustrates only too well the devastating effect mitochondrial disease can have.

But what are mitochondrial?

In every cell in the body, mitochondrial, which contain their own DNA, produce the energy that cells need in order to function effectively. In this respect they are often described as miniature power stations and the higher functioning the cell is, the more mitochondrial there are. There are, however, occasions where mitochondrial do not produce enough energy which in turn compromises the cell's ability to work effectively with tragic results. Given that some areas of the body such as the brain, heart and muscles demand high levels of energy, it is often organs such as the heart, brain and kidneys that are affected. Mitochondrial disease can lead to conditions such as seizures, dementia, early strokes, liver disease and Fanconi's Syndrome to name just a few.

The current law

The area of assisted reproduction in England and Wales is governed by the *Human Fertilisation and Embryology Act (HFE Act)* 1990 as amended by the 2008 Act. The HFE Authority was set up by the Act as its regulator with its primary function to consider and grant

[1] http://www.bbc.co.uk/news/magazine-19648992

licences to clinics and centres of research for assisted reproductive techniques. The current law is clear and unambiguous, and section 3 (1) of the Human Fertilisation and Embryology Act 1990 underlines the principles that an embryo cannot be created without a licence. Section 3(1) (a) governs the storage and use of the embryo intended for human application, moreover, if any activity is carried out without a licence, section 41 imposes criminal sanctions triable on indictment with a maximum penalty of 10 years imprisonment and/or a fine.

Only embryos and gametes as defined by the *Human Fertilisation and Embryology Act 1990,* section 1 (as amended), can be used to bring about the creation of an embryo. It is therefore the case that mitochondrial donation is not permitted by current legislation. However, section 3ZA (5) of the Human Fertilisation and Embryology Act 2008 inserted a new provision into the 1990 Act and states that '*regulations may provide that—*

(a)an egg can be a permitted egg, or

(b)an embryo can be a permitted embryo,

even though the egg or embryo has had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease'.

Thus, the 2008 legislation permits the introduction of regulations for mitochondrial donation and the creation of what is colloquially referred to as 'three parents, one baby' by way of in vitro fertilisation (IVF). It is these regulations which are discussed below.

The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015

The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (permitted by the 2008 amendments above) state that a permitted egg will now include one which is '*defined in section 3ZA (2) (b) of the Act and was extracted from the ovaries of a different woman'*[2], that is, the donor woman.

The creation of an egg by way of mitochondrial donation will be permitted where the HFE Authority is satisfied there is a particular risk that the mother's egg may have mitochondrial abnormalities caused by mitochondrial disease *and* there is a significant risk that the abnormalities will have or develop mitochondrial disease[3]. Thus, the Regulations will amend

[2] Section 3(a) (i) and section 3 (a) (ii) Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015

[3] Section 5 Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015

the meaning of a permitted egg within the Human Fertilisation and Embryology Act 2008 to include an egg that has been donated by another woman where there is a risk that the mother's egg may have mitochondrial abnormalities which in turn will risk the development of mitochondrial disease.

It is worth noting the terms 'particular risk'[4] and 'significant risk'[5] suggest there need not be actual certainty that the mother's egg does indeed contain faulty mitochondrial for mitochondrial donation to be carried out, simply a reasonably high level of risk is likely to be sufficient.

In this respect the wording is no different from the Human Fertilisation and Embryology Act 1990 which states that a licence cannot be authorised for embryo testing by way of pre implantation genetic diagnosis or PGD[6] unless there is a '*particular risk that the embryo may have any gene, chromosome or mitochondrion abnormality'*[7]*.* Once the 'particular risk' is established the HFE Authority can authorise the testing of the embryo once it is established that, in relation to that 'particular risk,' there is a significant risk of *'serious physical or mental disability, a serious illness or other serious condition'*[8]*.*

What amounts to a *'serious'* disability, illness or condition is perhaps easily apparent as some of the conditions associated with mitochondrial disease are by their very nature 'serious' and the Act (which the Regulations will rely upon) appear to accept some objective assessment where the term 'serious' is concerned.

Part 3 of the Regulations will only enable children born by way of mitochondrial donation to be able to access limited non identifying information about their mitochondrial donor, who in turn will only be able to obtain limited non identifying information about the child born as a result of their mitochondrial donation. In this sense, there is a clear difference from the information that will be released where mitochondrial donation is concerned, in contrast to other gametes donors where more information can be disclosed.[9]

In many respects, the Human *Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015* utilises the boundaries that have already been set by the HFE Authority

[4] Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 Section 5(a)(i)
[5] ibid Section 5(a)(ii)
[6] PGD is an assisted reproductive technique whereby a cell(s) is removed from a fertilised embryo to test for genetic abnormalities. If these are detected, the embryo will be discarded and destroyed or used for embryo research.
[7] Human Fertilisation and Embryology Act 1990 Schedule 2, section 1ZA(1)(b)
[8] Ibid Schedule 2, section 1ZA (2) (b)
[9] By way of The Human Fertilisation and Embryology Authority (Disclosure of Donor Information) Regulations 2004.

when embryo testing was permitted where there was a significant risk that a baby would be born with a serious disability or condition. The new Regulations will now permit mitochondrial donation where there is a significant risk of mitochondrial abnormality.

How mitochondrial donation would work in practice.

Perhaps the easiest way to describe a complex medical process is to break it down into a series of easy follow steps.

Firstly, picture a mother's egg which contains a nucleus which in turn contains the genetic information (the DNA) of the mother. Imagine that this nucleus is surrounded by faulty mitochondrial which must not pass to the embryo for fear of transferring mitochondrial disease.

Secondly, the healthy nucleus is removed. The remaining egg which has no nucleus and contains only faulty mitochondrial is destroyed or used for research. Next, the healthy nucleus of the mother's egg is transferred into a donor cell of a second woman which has had its own nucleus removed leaving behind only healthy mitochondrial (which also contains some DNA). The healthy nucleus of the mother and the healthy mitochondrial of the donor creates a new egg which is now ready to be fertilized with the sperm of the intended father by way of IVF.

Ethical issues

One of the most vociferous arguments against mitochondrial donation is also one of the most media attractive, but alarmist and inaccurate arguments. It is argued that if we were to permit mitochondrial donation we begin the slippery slope towards genetic engineering and designer babies. Although the memories of such attempts now reside in the recent past of World War 2, the argument is wholly inaccurate and misleading. The allegation that mitochondrial donation is a form of genetic engineering is a fallacy. The DNA inside a mitochondrial cell is a tiny amount, some 0.2% of the total DNA, only 37 of the some 25,000 genes in total and which contain no personal characteristics but whose purpose it is to power the mitochondrial cell itself.

Mitochondrial donation does not allow for selection of specific characteristics in relation to intelligence, sporting prowess or brilliantly blue eyes; mitochondrial donation only permits the exclusion of serious disability transmitted via faulty mitochondrial. Whilst it is correct to say the additional tiny amount of DNA from the donor cell will alter the germline permanently and passed down to subsequent generations, mitochondrial donation is intended to allow parents to have a child who will not suffer from a serious disability in the same way as pre

implantation genetic diagnosis tests an embryo for a specific disability or abnormality. The additional DNA from the donor cell is such an insignificant amount, should this really be something we should argue is so ethically unacceptable so as not to be permissible?

Opponents argue that to change the law and potentially risk the slippery slope towards designer babies for the benefit of a few mothers is not something that should be pursued. But why not? One of the purposes of medical research into assisted reproductive techniques is to benefit mothers who may have babies with serious disability which can be avoided in ways such as PGD and Tissue tying[10] and any opportunity to do so should be embraced. It is also the law's role to respond and if it thinks fit, to legislate appropriately in order to meet new medical technologies. The fact that these Regulations respond to medical advancement is something to be applauded and not remiss in the originally drafted legislation. It is often the case that the law follows medical advances or to amend the law to respond to new situations[11]. The law therefore is often a pace behind medical advances but it reacts promptly to ensure that tightly worded legislation is drafted not only to permit technology but also to ensure that it cannot be abused.

However, opponents also argue that the additional introduction of just a minute amount of additional DNA changes who we are and introduces a new being which challenges the very question of what amounts to an identity. However, this does not stand up to close scrutiny – the DNA from the donated mitochondrial will not affect appearance or physical similarities to the baby's mother or father and is unlikely that any child born as a result will question who they really are and feel harmed as a result. The alternative to this process is, of course, being born with a mitochondrial disease where it would appear the greater harm will be caused.

It is argued that the research is rushed and more time should be taken to consider various difficulties that may arise. However, research has been taking place for at least 7 years and research scientists feel confident that they are ready to begin using this technique for the benefit of mothers who carry faulty mitochondrial.

As with other technologies that seek to eliminate serious conditions pre IVF, there are concerns about the message that is sent regarding society's acceptance of those who have

[10] HLA (Human Leukocyte Antigen)

[11] Take for example, the Human Fertilisation and Embryology Authority (Disclosure of Donor Information) Regulations 2004 which was introduced to permit those born as a result of gamete donation the right to obtain certain information about the donor. Perhaps even more pertinent to this discussion would be the amendment in the Human Fertilisation and Embryology Act 2008, Schedule 2, paragraphs 1ZA (1) which permits pre implantation genetic diagnosis (PGD), a new assisted reproductive technique which was hardly envisaged when the 1990 Act was first drafted

a disability. If we are to discard a cell because it contains faulty mitochondria, then some may argue we are saying that disabled lives are not worth living. However, it is not that disabled lives are worthless but it is simply preferable to choose to have a baby that is healthy rather than a baby that will suffer from some serious disability[12]. In this respect, John Harris argues that it is preferable to prevent harm being caused and therefore acceptable to select against a disability[13]. It must also be remembered that eliminating faulty mitochondrial in an egg is carried out at the earliest stage possible, far sooner than embryo screening for disability, and not forgetting there is always the availability of late abortions to avoid serious disability[14].

In conclusion it is likely that the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 will pass through Parliament unrestrained so giving the hope to a small but significant number of mothers to be able to bear a child without passing on serious mitochondrial diseases.

[12] Buchanan A, Brock D, Daniels N and Wikler D, From Chance to Choice, Genetics and Justice, Cambridge University Press 2006

[13] Harris, J. Is there a social conception of the disability? 2000 26 Journal of Medical Ethics 95

[14] Section 1(1)(d) Abortion Act 1967