MITOCHONDRIAL DISEASE: THE NEED FOR MITOCHONDRIAL DONATION

Mitochondrial disease is a debilitating genetic disorder that robs the body's cells of energy, causing multiple organ dysfunction or failure and sometimes death. Mitochondrial disease occurs when a person's mitochondria are not working properly and can develop at any age from birth onwards.

Approximately 1 in every 200 Australians or around 120,000 people carry a genetic mutation that could potentially lead to mitochondrial disease developing and 1 in 5,000 babies are born with a severely disabling form of mitochondrial disease that can cause death in infancy, childhood or adulthood.

The Australian Mitochondrial Disease Foundation (AMDF), leading international and domestic experts, patients, carers and doctors, are working together to allow parents to reduce the risk of their children developing mitochondrial disease and prevent it being passed on through future generations.

MITOCHONDRIA

Mitochondria are small structures, found in our cells, which generate the energy that powers every part of our body. Mitochondria are often called the 'powerhouses' that provide us with all the energy our body needs to walk, talk, laugh, hear, digest food, function and breathe.

All cells in the human body have mitochondria, except for red blood cells. Mitochondria have their own DNA, which controls their function and, critically, energy production. This is separate from our nuclear DNA, which informs who we are, our appearance and our personality.

MITOCHONDRIAL DISEASE

Mitochondrial disease is a debilitating genetic disorder. Depending on the person and the form of their mitochondrial disease, they may suffer a whole range of symptoms from loss of motor control, strokes, seizures, visual or hearing problems, cardiac and/or liver disease, developmental delay and intellectual disability.

In some cases, mitochondrial disease is caused by genetic mutations in the nuclear DNA we inherit equally from our mother and father. Mitochondrial disease can also arise as a spontaneous genetic mistake at conception.

However, in about half of all known cases, mitochondrial diseases are caused by mutations in the separate mitochondrial DNA (mtDNA) that we inherit only from our mother. About 1 in 200 people (or approximately 120,000 Australians) carry a mutation in their mitochondrial DNA that could potentially cause disease and it is likely that mtDNA disease is much more common in the community than previously thought.

PEOPLE WITH MITOCHONDRIAL DISEASE

There is no one age group affected by mitochondrial disease. Babies can be born with it while other people develop it later in life, in early childhood, in their teenage years or as adults.

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IMPACT OF MITOCHONDRIAL DISEASE

The impact of mitochondrial disease can be devastating and virtually all forms of it have significant impact on patients.

Babies and young children die of Leigh disease, whilst other types of mitochondrial diseases can impact sufferers in different ways. Repeated seizures and loss of motor control can mean that people of all ages have to stop working and may need full time care which in turn can impact their family and friends.

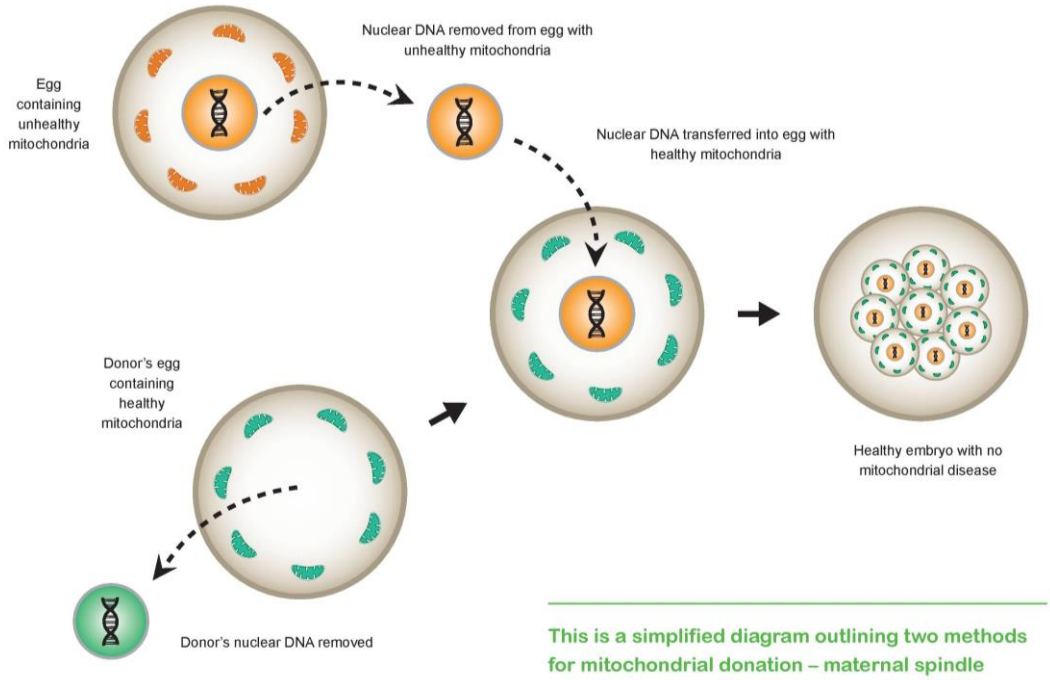
Many people with mitochondrial disease have repeated and/or prolonged visits to hospital. Symptoms can include temporary blindness, mitochondrial strokes, balance difficulties and digestive or eating difficulties, all requiring significant treatment and care. Patients may rely heavily on the healthcare, and sometimes social services, system.

PREVENTING MITOCHONDRIAL DISEASE FROM BEING PASSED ON

It is possible to significantly reduce the risk of mitochondrial disease being passed on. Mitochondrial disease caused by mistakes (mutations) in one of the nuclear genes involved in mitochondrial function can be prevented through prenatal testing or an IVF based procedure called preimplantation genetic diagnosis.

These approaches are generally not as reliable when the mutation is in mitochondrial DNA inherited from the mother. Mitochondrial donation is an alternate approach.

Mitochondrial donation, also known as mitochondrial transfer or replacement, can occur in one of two ways, both involving IVF. One technique involves transferring the nuclear genetic material from the affected mother's egg into a donor egg that has had its nuclear DNA removed and retains only its healthy mitochondrial DNA. The other, which has been approved in the UK, involves taking the nuclear DNA from a fertilised egg containing faulty mitochondria and transporting it into a fertilised donor egg with healthy mitochondria.



This is a simplified diagram outlining two methods for mitochondrial donation – maternal spindle transfer (prior to fertilisation) and pronuclear transfer (after fertilisation).

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INTERNATIONAL EXPERIENCE WITH MITOCHONDRIAL DISEASE

After many years of consultation, the use of mitochondrial donation was approved by the UK Parliament in 2015. In March 2017, the first clinical mitochondrial donation licence was granted to the Newcastle Fertility Centre at the International Centre for Life in Newcastle-upon-Tyne, United Kingdom.

The centre will now begin recruiting patients. The first child born via mitochondrial donation in the UK could be born as early as 2018.

THE AUSTRALIAN SITUATION

The key federal laws governing research and clinical practice in relation to embryology are the *Prohibition for Human Cloning for Reproduction Act 2002* and the *Research Involving Human Embryos Act 2002*.

Whilst there are a few sections of the laws that are relevant, the clauses critical for mitochondrial donation currently prohibit implantation of a human embryo that contains more than two people's genetic material regardless of whether that material is simply transferred, as in mitochondrial donation, or where genetic modification is proposed.

WHAT NEEDS TO CHANGE

Changing the law is critical to allow affected individuals the capacity to eliminate the risk of passing genetically associated mitochondrial disease to their children.

The AMDF, together with patients, carers and leading international experts, is calling on the Australian Government to change the necessary laws to enable mitochondrial donation by affected parents to ensure that their children are not placed at risk of mitochondrial disease.

HOW MANY PEOPLE WOULD BENEFIT?

The New England Journal of Medicine, in an article entitled Mitochondrial Donation – How Many Women Could Benefit, estimates that "the average number of births per year among women at risk for transmitting mtDNA [mitochondrial DNA] disease is 152 in the United Kingdom and 778 in the United States."

A simple extrapolation from the UK means that there are around 56 children each year in Australia who could potentially benefit from this technique, given the respective population sizes and assuming roughly equal age distribution and fertility.

Whilst this may seem a relatively low number, it represents a significant burden to our health system and a major burden and fear on behalf of families at risk. Conversely, eliminating this risk does not represent a significant cost or burden to the financial sustainability of the health system and would provide parents and families a choice in regards to the health risks facing their child.

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NEXT STEPS

In 2010, the then Federal Minister for Mental Health and Ageing, the Hon Mark Butler MP, appointed an independent committee to review the two relevant acts: the *Prohibition of Human Cloning for Reproduction Act 2002* and the *Research Involving Human Embryos Act 2002*. The Committee's report, released in July 2011, recommended the existing legislation remain the same.

In the intervening five years, the science behind mitochondrial donation has developed considerably with the techniques being enhanced and rigorously tested within the laboratory. This, and the fact that licenses to perform mitochondrial donation are likely to be issued shortly in the UK, provide the confidence to now look to bring the same opportunities to Australian parents and their families.

The NHMRC is currently reviewing the legislative framework around embryo research. Its aim is to provide a document to the Minister for Health regarding recent scientific advances that impact the legislation and other changes or developments from around the world that are relevant, such as the UK example. This offers a significant opportunity for the Government to review Australia's laws to give parents the choice to have their children free from this devastating and life-threatening disease.

The AMDF calls on the Australian Government to legalise mitochondrial donation, giving women who carry these genetic mutations the choice to eliminate the risk of their children inheriting this devastating and life-threatening disease.

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