

MITOCHONDRIAL DISEASE: THE NEED FOR MITOCHONDRIAL DONATION

Mitochondrial disease (known as mito for short) 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 Mito Foundation (incorporated as the Australian Mitochondrial Disease Foundation), 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.

WHAT CAUSES MITOCHONDRIAL DISEASE?

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.

IMPACT OF MITOCHONDRIAL DISEASE

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

Mitochondrial disease can cause any symptom, in any organ, at any age.

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.

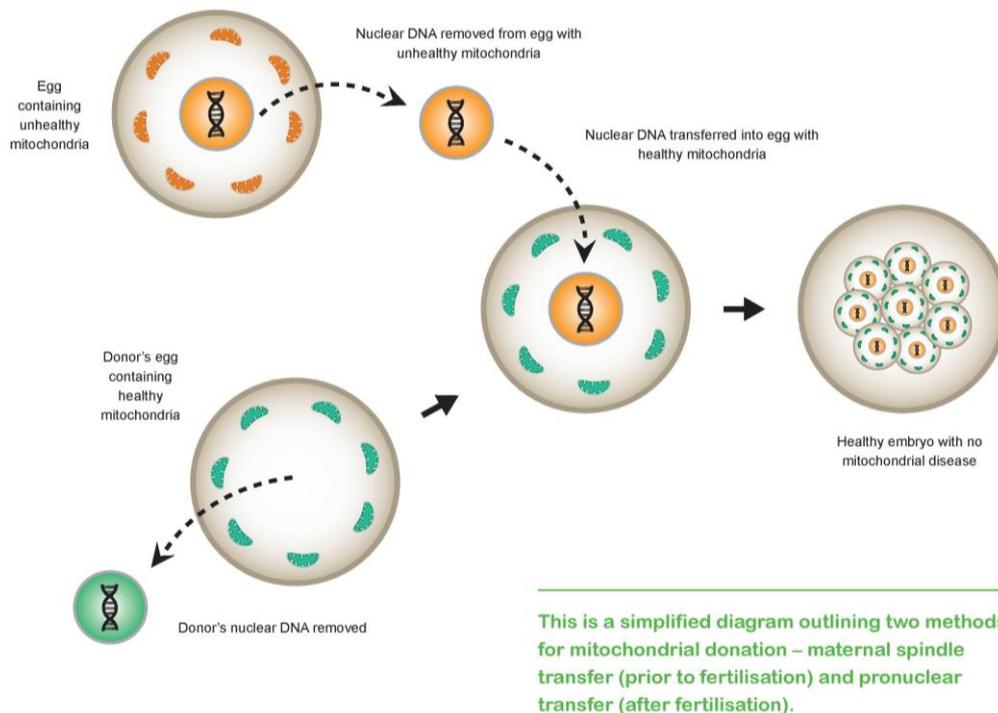
Many people with mitochondrial disease have repeated and/or prolonged visits to hospital. Symptoms can include vision loss, mitochondrial strokes, balance difficulties and digestive or eating difficulties, all requiring significant treatment and care. Patients may rely heavily on the healthcare, and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

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.



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.

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.

In February 2018 the first licences were granted to two women to undergo mitochondrial donation at the Newcastle Fertility Centre. The first child born via mitochondrial donation in the UK may arrive as early as 2018. Due to privacy constraints it is unlikely that the births will be announced.

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.

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 eight 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 have already been issued in the UK, provide the confidence to now look to bring the same opportunities to Australian parents and their families.

The NHMRC has reviewed the legislative framework around embryo research. It has provided 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 offered 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.

Following a Senate Inquiry, on 27 June 2018, a Senate Committee recommended a pathway to legislative change to allow Australian parents the opportunity to have children free of maternally inherited mitochondrial disease.

The Committee's report has been welcomed by the Mito Foundation.

As of 22 November 2018, the Australian Government has not responded to any of the five recommendations made in the Report. The Government has not prepared a consultation or sought advice from the National Health and Medical Research Council (NHMRC), as per the first recommendation in the Senate Report.

The Mito Foundation and members of the mito community are disappointed in the lack of progress that has been made in the last five months. To read the Senate Report visit:

www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/MitochondrialDonation/Report

NEXT STEPS

The Mito Foundation strongly encourages the government to address the five recommendations from the Senate Report as a matter of urgency.

Between 27 June 2018, when the Report was released and 22 November 2018, 23 babies have been born that may develop a life threatening form of mitochondrial disease and experience devastating symptoms.

The Foundation is calling on MPs to indicate their support of mitochondrial donation and write to the Minister of Health requesting urgent action be taken on the recommendations.

For more information, please contact Rebecca Davis at the Mito Foundation on 20 8033 4113 or rebecca.davis@mito.org.au or visit www.mito.org.au/mitochondrial-donation

The Mito Foundation 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.