

What is mitochondrial disease?

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How are sufferers affected?

Who is affected?

How common is mitochondrial disease?

How is it diagnosed and treated? Is there a cure?

Links with ageing and major diseases

Why haven't we heard much about mitochondrial disease before?

What is mitochondrial donation?

Australian legislation governing mitochondrial donation

Australian Mitochondrial Disease Foundation

What is mitochondrial disease and what causes it?

Mitochondrial disease (mito) is a debilitating genetic disorder that starves the body's cells of energy, causing multiple organ dysfunction or failure and potentially death. Most patients have a genetic change in their mitochondrial DNA or nuclear DNA. The condition can be inherited from the mother, the father, or both parents, or can arise as a spontaneous genetic mistake at conception.

What are mitochondria?

Mitochondria are the energy source in almost every body cell. Often called the cells' powerhouses or generators, mitochondria transform food to produce 90 per cent of the energy needed by the human body to function, sustain life and support growth. Mitochondria are most plentiful in tissues that require a lot of energy to function; the disease therefore causes most damage to the cells of the brain, muscles, heart, liver, inner ear and eye.

How are sufferers affected?

Depending on which parts of their bodies are affected and to what degree, people with mitochondrial disease can:

- lose their sight or hearing
- suffer muscle weakness and pain
- be unable to walk, eat, swallow or talk normally
- have strokes or seizures
- develop liver disease or diabetes
- suffer heart, respiratory or digestive problems
- experience developmental delays or intellectual disability.

Needing to regularly rest and recharge is a common outward symptom of mitochondrial disease. Inside the body, it's much more serious and complex: **mitochondrial disease may cause any symptom in any organ at any age.**

Who is affected by mitochondrial disease?

Mitochondrial disease can affect both **children and adults**; due to its genetic basis, the disease often affects **multiple family members**. Adult onset is becoming more commonly recognised. In many cases, the impaired mitochondrial load (cell injury and cell death) increases with age, until organ systems begin to fail and symptoms develop.

How common is mitochondrial disease?

Until the 1990s, mitochondrial disease was thought to be rare (1 in 20,000 people), but it is now recognised as the most common subgroup of inherited metabolic disorders. Recent research shows **1 in 200 people, or more than 120,000 Australians**, may carry genetic changes that put them at risk for developing mitochondrial disease or other related symptoms such as diabetes, deafness or seizures during their lifetimes. Many of these people are symptomatic but undiagnosed or misdiagnosed, some are not yet symptomatic, and others are unknowingly at risk of passing the disease on to their children.

Put another way, up to 30 children born in Australia each week – or 1540 children a year – are at risk for developing a mild to moderately disabling form of mitochondrial disease, while at least one Australian child born each week – or 62 children every year – will develop a severe or life-threatening form of mitochondrial disease (1 in 5000 people), making it the second most commonly diagnosed serious genetic disease after cystic fibrosis, which has an incidence of around 1 in 3500 people.

How is mitochondrial disease diagnosed and treated? Is there a cure?

Mitochondrial disease is a complex condition that is **difficult to diagnose** due to the widespread range, type and severity of symptoms and its varying onset and impact on patients' lives (from none to severe). Multiple tests may be required to confirm mitochondrial disease, including genetic tests, muscle biopsies or brain scans (depending on the type of disease suspected).

There are **currently very few effective treatments** and as yet **no cure for mitochondrial disease**. It impacts differently on every patient, so doctors can't predict the progression of the disease or symptoms, or the outcome for patients.

Why haven't we heard much about mitochondrial disease before?

Mitochondrial medicine is a newly established and rapidly evolving field thanks to major advances in our understanding of genetics. **It was not until 1988 when changes in mitochondrial DNA were discovered to cause disease**, and 1995 when nuclear DNA changes were also found to cause mitochondrial disease. Since then, **more than 100 clinical syndromes and disorders** have been recognised as coming under the category of mitochondrial disease.

Links with ageing and major diseases

Whereas people with mitochondrial *disease* have a genetic change that predisposes their mitochondria to fail early, **mitochondrial dysfunction is now thought to be one of the major factors contributing to ageing** and the reason why humans have a finite lifespan. Over a lifetime, our mitochondria slowly suffer inevitable damage from environmental and lifestyle factors and become less effective at producing the energy our organs need to function properly.

Researchers increasingly believe mitochondrial dysfunction may be a significant factor in a wide range of major diseases – particularly chronic degenerative disorders and those associated with ageing – including:

- Parkinson disease
- Alzheimer disease
- Huntington disease
- motor neurone disease / amyotrophic lateral sclerosis (ALS)
- cardiovascular disease
- diabetes
- cancer, particularly solid tumours and tumour metastasis (spread to other organs).

Research into mitochondrial medicine therefore offers hope not only to people with primary mitochondrial disease (due to a genetic mutation), but also to the millions suffering from other major diseases commonly associated with ageing. Improvements in mitochondrial medicine may eventually provide **the key to better health and quality of life in old age for all**.

What is mitochondrial donation?

Mitochondrial donation (also called mitochondrial replacement therapy) is an in-vitro fertilisation (IVF) technique to prevent transmission of maternally inheritable mitochondrial disease from mother to child – that is, forms of the disease caused by changes in the mitochondrial DNA, which a child inherits only from its mother.

The procedure involves transferring 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. This can be done before or after the mother's egg is fertilised, called maternal spindle transfer or pronuclear transfer respectively.

Almost all or 99.9 per cent of the resulting baby's genetic material is nuclear DNA, contributed equally by the biological mother and father – more than 20,000 genes that determine the child's appearance, intelligence, behaviour and other personal characteristics.

A tiny fraction or 0.1 per cent is mitochondrial DNA from the donor egg, in place of the mother's faulty mitochondrial DNA – 37 genes that regulate how the baby's cells convert food and oxygen into the energy needed to power its organs.

Mitochondrial donation can be compared to changing the sparkplugs in an engine or a transplant into a patient with organ failure.

After extensive research and a comprehensive global scientific and ethical review of mitochondrial donation over a ten-year period in the United Kingdom, the UK Parliament approved legislation in 2015 to allow the procedure.

The UK has now established the world's first regulated system to provide mitochondrial donation. It is overseen by the Human Fertilisation and Embryology Authority (HFEA), which licenses clinics and reviews patient applications to undergo the procedure.

In February 2018, two UK women carrying mitochondrial DNA changes were granted permission to undergo mitochondrial donation, giving them the opportunity to have healthy children.

Australian legislation governing mitochondrial donation

Legislative change is required to allow affected Australian couples the choice to use the technique, enabling them to have biological children who will not suffer the disabling and potentially deadly consequences of severe mitochondrial disease.

In all states except Western Australia, research on a limited range of mitochondrial donation is permissible up to day 14 of embryo development, subject to a licence being granted. Following a review by an independent committee of the two relevant acts in 2010, it was recommended the existing legislation remain unchanged.

Mito Foundation is calling on the Australian Government to revise its legislation and give women the choice to access mitochondrial donation in Australian IVF clinics.

For the latest news on the initiative please visit: www.mito.org.au/mitochondrial-donation

The Australian Mitochondrial Disease Foundation (AMDF)

AMDF is now known as the Mito Foundation. It is still incorporated as AMDF.

The Australian Mitochondrial Disease Foundation was set up in 2009 by family members, friends and doctors of sufferers. Mito Foundation supports sufferers and their families, funds essential research into the prevention, diagnosis, treatment and cure of mitochondrial disorders, and increases awareness and education about this devastating disease. The organisation does not receive government funding and relies solely on donations.

Mito Foundation funds numerous research projects, an Australia-wide mitochondrial patient database and priority access to a new Next-Generation DNA Sequencing Facility to enable faster, less expensive and more accurate diagnoses of mitochondrial disease.

Mito Foundation operates a Helpline (1300 977 180), runs support services including Mito Connect Calls, support groups, and a Facebook group, and holds Mito Information Days and symposia for patients, GPs, specialists and the public.

Global Mitochondrial Disease Awareness Week (gmdaw.org) takes place in the third week of September each year and includes a variety of education and information sessions, fundraising activities, and support and advocacy initiatives.

Major Mito Foundation fundraising and awareness events include **The Bloody Long Walk** national series (bloodylongwalk.com.au) and **Stay in Bed Day** (stayinbedday.org.au), conceived because being forced to stay in bed to rest and recharge is a common outward symptom of mitochondrial disease (and because we all enjoy a sleep-in once in a while). Other initiatives to support the mitochondrial disease cause are held during the year by Mito Foundation, groups and individuals.

This fact sheet has been reviewed by Mito Foundation's Scientific and Medical Advisory Panel. It is for general information only and should not be relied on for medical decisions.