BENEFITS OF A GENETIC DIAGNOSIS OF MITOCHONDRIAL DISEASE

The benefits of a genetic diagnosis include:

- Enabling access to treatment and symptom management pathways to alter the progression of the disease
- Providing relief and dignity for patients and families by ending the diagnostic odyssey
- Facilitating access to financial and other relevant support, and assists individuals and families in planning for the future
- Enabling patients to make informed decisions about reproduction and accessing reproductive technologies

The Australian Mitochondrial Disease Foundation (AMDF) believes that people who are suspected of having a mitochondrial disease (mito) should undergo testing to receive a formal genetic diagnosis.

This document is aimed at clinicians and outlines the benefits of receiving a genetic diagnosis.

Probably fewer than a third of individuals with mito receive a definitive diagnosis. Due to there currently being few effective treatments and no cure, many physicians do not pursue a formal diagnosis, despite the benefits it will have for individuals and their families.

Securing a diagnosis can ensure patients receive a coordinated healthcare approach and justify their support needs.

Advances in genetic testing mean that obtaining a genetic diagnosis is more accessible than ever before. Previously, receiving a diagnosis could take months, if not years and have significant cost implications to patients, and to the healthcare system. Tests such as muscle biopsies can be painful and invasive, are often inconclusive, and may pose a risk for patients sensitive to anaesthetics.

Eligible patients may be able to access genetic testing through an Australian Genomics Health Alliance (AGHA) initiative, which is being co-funded by AMDF. Please contact AMDF for more information on 02 8033 4113.

Enables access to optimal care to potentially alter disease progression

Whilst there are few effective treatments and no cure, there are recommendations for managing symptoms and optimising mitochondrial health to slow disease progression and improve quality of life.

Depending on the diagnosis and symptoms, these can include:

- Lifestyle changes to prevent fatigue
- Good nutrition to ensure optimum mitochondrial function
- Avoidance of cigarette smoking
- 'Mito Cocktail' of supplements which may include Co-enzyme Q10, L-arginine, vitamin C, D, E and K, riboflavin and idebenone [1]
- A tailored aerobic exercise program to improve muscle fatigue symptoms and muscle performance [1]
- Avoidance of occupational or excessive recreational noise to prevent hearing loss [1]

Provides relief for the individual

A delayed diagnosis (5–30 years) is reported in 25–40 per cent of cases of rare diseases and 40 per cent are initially given an incorrect diagnosis.[2] The diagnostic journey is a time of uncertainty, anxiety and isolation. A diagnosis provides individuals with an explanation of their symptoms and helps to validate their experience.

It prevents individuals from undergoing unnecessary tests and therapies which are often costly and painful. Patients without a diagnosis may seek unproven alternative therapies, increasing financial burden and emotional stress.

Case Study

Dr Karen Crawley is a General Practitioner whose eldest daughter Kara has Mitochondrial Encephalopathy, Lactic Acidosis and Stroke-like Episodes (MELAS).

"From birth until she was finally diagnosed at eight years old, I was often given the impression that I wasn't handling my daughter correctly and that I was the cause of her problems and quirkiness. Kara was the extreme of normal in all aspects of her health, so every time I questioned something, I was told that she didn't have an 'illness' and that Kara was simply 'hard work'.

So when the diagnosis was finally given it was an incredibly huge and heart wrenching shock. We were told that our little girl was going to suffer repeated strokes, slowly lose all her functions (mind and body), suffer much pain and slowly die over the next 2-10 years. However, this devastating news was nothing compared to all those years of not knowing what was happening and being led to believe that we were imagining things. I would swap all those painful years of not knowing, for knowing. They are years we can't get back and we have been left with intense guilt for following the advice to push her harder to do things, when mito was the reason she couldn't."

Provides dignity for patients

A diagnosis provides patients with the ability to explain their symptoms, which can be broad and seemingly unrelated.

Some mito patients have been labelled as hypochondriacs, while fabricated or induced illness by carers (FIIC), has been suggested as an explanation for the complexity of symptoms experienced by some children.

Symptoms such as extreme fatigue can prevent individuals from participating in activities. With no explanation as to why they are so exhausted, relationships can be impacted, leading to further isolation and potentially impacting their mental health. Patients with mito who are employed are left unable to justify recurrent sick leave or their need for flexible work requirements.

"I've seen the relief on patient's faces and their self-esteem rise when they are told that it isn't in their head and that there is a real and valid reason why they feel the way they do. Diagnosis reinstates a patient's dignity." - Dr Karen Crawley, General Practitioner

A lack of a unifying diagnoses not only causes individuals to feel frustrated and helpless, it can also negatively impact on their clinician and the clinician-patient relationship[2].

Ensures eligibility for government support

A diagnosis is important and in some cases essential in enabling individuals to access government support services, including financial assistance.

Symptoms may prevent sufferers from working. The Centrelink Disability Support Pension requires evidence of a physical, intellectual, or psychiatric impairment resulting in the inability to work for a minimum of 15 hours per week, over the coming two years.

A diagnosis also facilitates applications for the Child Disability Allowance and Carer's Allowance, as evidence is required regarding the level of care needed. Whilst the National Disability Insurance Scheme (NDIS) is based on an individual's level of disability, a diagnosis can provide the evidence needed to verify that the disability is permanent and the need for support is lifelong. A definitive diagnosis can expedite the application process and avoid questions around the illness, leaving the onus on the patient to prove their disability. This can involve the collection of reports from multiple specialists, undergoing invasive questioning, and waiting months for an outcome – all while dealing with their ongoing symptoms and increasing financial burden.

"After years of struggling with unexplained fatigue, muscle pain and other symptoms I had to leave my job. I had no financial support and we had to live off my husband's wage. When I was finally diagnosed with mito, I was able to claim my total permanent disability (TPD) from my superannuation. Getting my diagnosis also helped with getting my mum

diagnosed, which enabled her to access the disability pension and my dad to receive a carers allowance as her full time carer." – Melissa Armstrong who has Chronic Progressive External Ophthalmoplegia (CPEO). Read her case study on accessing TPD.

Enables individuals to make informed decisions around reproduction and accessing reproductive options

A diagnosis, combined with genetic counselling ensures couples who are at risk of transmitting mito to their future children, are able to make an informed decision.

Pre-implantation genetic diagnosis (PGD) is an IVF technique which can be used to test embryos for known genetic abnormalities including certain types of mito. Only healthy embryos are selected for transfer during the IVF cycle, maximising the chances of a healthy baby.

"Trying to have another child without PGD would have felt like playing Russian roulette, as there was a one in four chance that he or she would inherit Leigh syndrome. Our son Dion's genetic diagnosis meant that we could prevent our other children from inheriting this awful disease."- Tracy and Warren Taprell's son Dion passed away from Leigh syndrome at just three years old. Dion's genetic diagnosis enabled them to have two healthy children using PGD. Read their case study on PGD.

Mitochondrial replacement IVF techniques (i.e. mitochondrial donation) are being developed to reduce the transmission of maternally inherited mito. They involve 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. The first license to use this technique was approved in the UK in 2016. AMDF is actively advocating for changes in legislation to give families access to mitochondrial donation in Australia.

Enables individuals to make informed decisions around reproduction and accessing reproductive options

Genetic counselling is recommended for relatives to provide information about the risk of inheritance and help them make an informed decision about undergoing testing themselves, particularly for those considering starting a family or who may themselves already be symptomatic.

Provides answers and enables individuals and families to plan for their future

Whilst it is difficult to definitively predict disease progression, having a diagnosis can help patients consider their needs and plan for their future. This may involve considering financial, housing and carer requirements.

A diagnosis can also help individuals and their families consider their personal values and preferences related to future healthcare and medical intervention. This may include an advanced care plan or directive.

Without a definitive diagnosis, individuals and their families are left uncertain about what the future may hold.

Ensures eligibility for clinical trials and other studies

AMDF is committed to facilitating an increase in the number of clinical trials taking place in Australia. It has established the first Australian Mitochondrial Disease Patient Registry, which will help to attract international clinical trials and will be an invaluable recruitment tool.

Contact AMDF for more information

AMDF believes that people who are suspected of having mito will benefit from a formal diagnosis and should undergo genetic testing

[1] Liang, C. & Sue, C., 2011. How to Treat: Mitochondrial Disease. Australian Doctor. pp27-34.
[2] Dudding-Byth, T., 2015. A powerful team: The Family Physician advocating for patients with a rare disease. Australian Family Physician. Vol.44, No.9, pp634-638