Chapter 2

Living with mitochondrial disease

> Mitochondrial disease is a horrible disease, and you wouldn't wish it upon your worst enemy.[1]

What is mitochondrial disease?

2.1 As outlined in chapter one, mitochondria are found in the fluid surrounding the nucleus of cells and are responsible for making energy within the cell. In order to work, the mitochondria have their own mitochondrial DNA[2] (mtDNA).

2.2 In about half of all known cases, mitochondrial disease is caused by mutations in the separate mtDNA that we inherit matrilineally (only from our mother). This form of mitochondrial disease is known as mitochondrial DNA disease. In other cases, mitochondrial disease is caused by genetic mutations in the nuclear DNA we inherit equally from our mother and our father. Mitochondrial disease can also arise as a spontaneous genetic mutation at conception.[3]

2.3 Mitochondrial disease is varied in presentation — it can be mild with little or no symptoms or can be severe enough to be life threatening. It tends to affect parts of the body that require a lot of energy, like the brain, muscles, kidney and heart.[4] Mr Sean Murray, Chief Executive Officer of the Australian Mitochondrial Disease Foundation (AMDF) told the committee 'there are hundreds of types of mitochondrial disease. Saying "mitochondrial disease" would be perhaps something like saying "cancer"'.[5]

2.4 AMDF summarised mitochondrial disease as:

> Mitochondrial disease is a debilitating genetic disorder that starves the body's cells of energy, causing multiple organ dysfunction or failure and potentially death. Mitochondrial disease occurs when a person's mitochondria are not functioning properly. It primarily affects the muscles and major organs, such as the brain, heart, liver, inner ears and eyes, but can cause any symptom in any organ at any age.
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> …
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> Depending on which parts of a person's body are affected and to what degree, people with mitochondrial disease may: have strokes or seizures; be

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1 Mr Sean Murray, Chief Executive Officer, Australian Mitochondrial Disease Foundation (AMDF), *Committee Hansard*, 17 May 2018, p. 1.

2 Deoxyribonucleic acid (DNA) is a chain of nucleotides carrying the genetic instructions for the growth, development, functioning and reproduction of living organisms.

3 AMDF, *Mitochondrial Disease: the need for mitochondrial donation*, p. 1.

4 House of Commons Library (UK), *Mitochondrial Donation*, Standard Note: SN/SC/6833, 29 January 2015, p. 5.

5 Mr Murray, *Committee Hansard*, 17 May 2018, p. 4.

> unable to walk, eat, swallow or talk normally; develop liver disease or diabetes; suffer heart, respiratory or digestive problems; lose their sight or hearing; suffer muscle weakness and pain; and experience developmental delays or intellectual disability.[6]

2.5 These diseases vary in presentation and severity, but common symptoms include developmental delays, seizures, weakness and fatigue, muscle pain, vision loss and heart problems, leading to morbidity and in some cases premature death.[7]

2.6 Professor John Christodoulou, Chair in Genomic Medicine at the Murdoch Children's Research Institute and the University of Melbourne Department of Paediatrics, told the committee that mitochondrial disease can be immediately present at birth, or can manifest itself later in childhood, or even as an adult:

> For instance, in some mitochondrial disorders, particularly those affecting children, children will appear to be normal for a period of time, maybe even for a few years, and then, when they have their very first major significant illness and their body needs additional energy to be made, they can't meet that need. That's when the disease may first manifest itself.[8]

2.7 Rhonda told the committee her families first experience of mitochondrial disease came without warning:

> Our first exposure to mitochondrial disease was when my brother was rushed to hospital with what we thought was a stroke. He was 34 years old. As part of determining what caused Peter's stroke, my whole family was tested and it was identified that my two brothers, two sisters, my mother and myself carried the defective gene.[9]

Lack of awareness

2.8 Submitters and witnesses told the committee there is a lack of awareness of mitochondrial disease even within the medical community, and this often leads to poor health treatment. AMDF told the committee that patients and parents of young children who have mitochondrial disease often 'feel like they're explaining what mitochondrial disease is to the medical community'.[10]

2.9 One submitter pointed to delayed emergency treatment due to this lack of awareness:

> I can be screaming in pain, and having my family tell them she has Mitochondrial Disease, just for them to question what the disease really is

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6 AMDF, *Submission 26*, p. 2.

7 Committee on the Ethical and Social Policy Considerations of Novel Techniques for Prevention of Maternal Transmission of Mitochondrial DNA Diseases: US Institute of Medicine, *Mitochondrial Replacement Techniques: Ethical, Social, and Policy Considerations*, February 2016, p. 1.

8 Professor John Christodoulou, Chair, Genomic Medicine, Department of Paediatrics, University of Melbourne, *Committee Hansard*, 17 May 2018, p. 13.

9 Rhonda, *Committee Hansard*, 17 May 2018, p. 33.

10 Mr Murray, *Committee Hansard*, 17 May 2018, p. 2.

> and how they should they treat me for the pain/reason I have presented to emergency.[11]

2.10 Another submitter outlined that after the birth of a family member, the Consultant Neonatologist at the neonatal intensive care unit at their hospital 'admitted that he needed a two-hour meeting with the [neonatal intensive care unit's] genetics/metabolics team to help him understand what this disease was all about and how it was affecting M because mitochondrial disease was such a rare, recently identified condition that he learnt nothing of it when he went through medical school'.[12]

2.11 Due to this lack of awareness, some people experienced a delayed diagnosis of mitochondrial disease:

> [Y]ou're underweight and you think it's just the case that you're genetically that way. Then you start losing your hearing and you think: 'Well, that's okay. We'll deal with that.' Then all of a sudden you have diabetes and you deal with that. You don't always put the picture together. For many people, it's a long, long time to come up with a diagnosis—many, many years.[13]

2.12 One witness, Rhonda, had a similar experience of delayed diagnosis in her family:

> With my brother's diagnosis, once he had his first stroke it was quite a quick diagnosis. But, as a teenager, he was diagnosed with having what was called a sleeping sickness. I mean, what is that? The doctors didn't know what it was. Before that, my grandmother had the same symptoms had the same symptoms [sic] as my mother, my brother and me. We just thought, 'Oh, well, she's hard of hearing and she's not quite right,' but there was no diagnosis. So I suppose, with mitochondrial disease in our family, the diagnosis hasn't exactly been quick. It's been hanging around for a long time.[14]

2.13 Others, particularly parents of children who died, did not receive a formal diagnosis until years later when other family members became symptomatic and underwent genetic testing.[15]

2.14 Professor Carolyn Sue, Director of the Mitochondrial Disease Research Centre at the Kolling Institute of Medical Research, leads a mitochondrial disease clinic at the Royal North Shore Hospital. Professor Sue told the committee that the referral patterns she sees in her patients, indicates that patients have 'hidden disease'

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11 Name Withheld, *Submission 32*, p. 2.

12 Name Withheld, *Submission 39*, p. 1.

13 Shelley, *Committee Hansard*, 17 May 2018, p. 38.

14 Rhonda, *Committee Hansard*, 17 May 2018, pp. 38–39.

15 Shelley, *Committee Hansard*, 17 May 2018, p. 38.

and she estimates on average, patients have seen eight to 10 doctors before coming to her clinic for a final diagnosis.[16]

2.15 AMDF echoed this view, telling the committee that:

> It's not uncommon for patients to have found their way to a mitochondrial disease diagnosis having spent 10 or so years bouncing around from one specialist to another… So the medical community is treating them and looking at their symptoms in silos, and it's not until somebody connects the dots of all of these symptoms that somebody suspects mitochondrial disease. In fact, it's not been uncommon for us to have patients report that they've ended up at a psychiatrist or a psychologist because the medical community says, 'There couldn't possibly be this many things wrong with you; it must be all in your head.'[17]

Rate of mtDNA mutation and mitochondrial disease

2.16 Because mitochondrial disease is poorly understood both in the general Australian community and within the medical professions, it is often thought of as a rare disease. However, AMDF told the committee it is more common than people think and 'it's estimated that one in 5000 people born will ultimately develop a life-threatening form of mitochondrial disease in their lifetime.'

2.17 AMDF further told the committee that at least one in 200 people carry one of the genetic changes in their mtDNA which can cause mitochondrial disease.[18] A groups of leading scientists in this field submitted that these carriers are likely to have 'symptoms that are common in the general population and unlikely to prompt suspicion of mitochondrial disease while these individuals are in the reproductive age group'.[19] The submission states that these carriers are likely to remain a 'hidden burden of mitochondrial disease, at least until community genetic screening becomes available that would detect people at risk of mitochondrial DNA disease'.[20]

2.18 Professor David Thorburn, Head of Mitochondrial Research and Diagnostic Laboratories at the Murdoch Children's Research Institute told the committee that:

> [W]e believe that about 60 children born in Australia each year will develop severe mitochondrial disease at some stage during their lifetime. I have helped to diagnose

16 Professor Carolyn Sue, Director, Kolling Institute of Medical Research, Mitochondrial Disease Research Centre, *Committee Hansard*, 17 May 2018, p. 26.

17 Mr Murray, *Committee Hansard*, 17 May 2018, p. 3.

18 Mr Murray, *Committee Hansard*, 17 May 2018, p. 2. It was later clarified that not all the 1 in 200 individuals will develop sever mitochondrial disease. See AMDF, *Submission 26.1*, p. 3.

19 Professors David Thorburn, John Christodoulou, Carolyn Sue, John Carroll, Mike Ryan and Aleksandra Filipovska, *Submission 59*, p. 3.

20 Professors Thorburn, Christodoulou, Sue, Carroll, Ryan and Filipovska, *Submission 59*, pp. 3–4.

> more than 600 children with mitochondrial disease, the vast majority of whom have died in childhood as our treatments do remain largely ineffective.[21]

2.19 Professor Sue provided evidence that the rates of mitochondrial disease in adults is largely unquantified:

> Our bottleneck is really how many patients we can fit in the clinic as to how many patients are out there, because I can tell you now that we won't be able to see a hundred thousand patients in our clinic in any one day or month. However, we know that patients are hidden in various different clinics—diabetic clinics, hearing loss clinics, cardiac clinics and probably infertility clinics as well—where patients have died without the cause being known.[22]

2.20 Professor Sue furthermore told the committee that the diagnosis rate of mitochondrial disease is likely to increase in coming years:

> We're looking at big data in trying to work out some of this, but the size of the problem is only going to grow, in my opinion. It has grown. The trajectory is going up. That's what I've seen from 20 years ago, and it's getting higher and higher. We're trying to work out ways to service those patients as much as trying to help them.[23]

Broader health impacts

> Many experts refer to Mitochondrial Disease as the 'Notorious Masquerader' because it wears the mask of many different illnesses.[24]

2.21 As outlined earlier in this chapter, mitochondrial disease often has a delayed diagnosis due to a lack of awareness in the medical community. It is increasingly the view of the medical and scientific community that mitochondrial disorders may be present in a larger range of illnesses than previously thought. AMDF contends that there is strong evidence that impaired mitochondrial function is important in Parkinson's disease, diabetes and diabetic complications. Disorders such as Alzheimer's, autism, cardiovascular disease and some forms of cancer have also been associated with mitochondrial dysfunction, as has the process of ageing.[25]

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21 Professor Thorburn, Head of Mitochondrial Research and Diagnostic Laboratories, Murdoch Children's Research Institute and Victorian Clinical Genetics Services, *Committee Hansard*, 17 May 2018, p. 11.

22 Professor Sue, *Committee Hansard*, 17 May 2018, p. 26.

23 Professor Sue, *Committee Hansard*, 17 May 2018, p. 26.

24 United Mitochondrial Disease Foundation, *Mitochondrial Disease in Adults*, http://www.umdf.org/mitochondrial-disease-in-adults/ (accessed 30 May 2018).

25 AMDF, *Mitochondrial Disease Information: Where does mitochondrial disease hide if it is NOT diagnosed*, https://www.amdf.org.au/mito-info/ (accessed 31 May 2018).

Diagram 2.1—Where does mitochondrial disease hide?

Source: AMDF, *Mitochondrial Disease Information: Where does mitochondrial disease hide if it is NOT diagnosed*, https://www.amdf.org.au/mito-info/ (accessed 31 May 2018).

Treatment

2.22 There are few effective treatments and no cures for mitochondrial disease. AMDF submits that this means the impacts on individuals and families of mitochondrial disease are devastating.[26]

2.23 Professor Christodoulou, a specialist in paediatric metabolic diseases and a clinical geneticist, told the committee that although the capacity to diagnose these diseases has been greatly enhanced in the past decade, 'where we've failed our patients has been in the identification and delivery of effective treatments for the vast majority of them'.[27]

Living with mitochondrial disease

2.24 As outlined earlier in this chapter, mitochondrial disease is a debilitating genetic disorder that can cause multiple organ dysfunction or failure and potentially death. It primarily affects the muscles and major organs, such as the brain, heart, liver, inner ears and eyes, but can cause any symptom in any organ at any age.

2.25 Professor Thorburn told the committee that of the approximately 600 children he has diagnosed with mitochondrial disease, the vast majority have died.

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26 AMDF, *Submission 26*, p. 2.

27 Professor Christodoulou, *Committee Hansard*, 17 May 2018, p. 12.

2.26 A mother whose child died of mitochondrial disease described her daughters condition:

> She had gone from the flourishing 8yr old, full of hope, dreams and motivation, to having dementia, deafness, partial blindness, tube feeds, incontinence, immobile, seizures, diabetes, multi-organ failure, dysphasia and extreme fatigue.[28]

2.27 The submitter went on to describe her work on a helpline:

> So many of the hundreds of patients and families I spoke to over those years, were like us, mortified, existing to survive now rather than live. Trying their utmost to create as many precious memorable moments, always looking for the smile in their child's or partner's face.[29]

2.28 A submitter described the symptoms of her mitochondrial disease, which in her case was categorised as mild:

> It currently causes extreme fatigue and pain in all my muscles. I have all my organs checked annually, visit my neurologist and an array of other health professionals regularly. I can't work full time anymore, can't exercise anymore and need a lot of sleep (10-12 hours a few times a week).[30]

2.29 A sibling of a man who died of mitochondrial disease submitted a list of his symptoms as 'loss of hearing, multiple stroke-like episodes, seizures, extreme fatigue, muscle wastage, cognitive impairment, poor balance and loss of motor skills. He also endured tonsil cancer and underwent radiotherapy which affected his voice, his saliva glands and the muscles in his neck which never recovered, leaving him with a permanently drooping head'.[31] This submitter listed the number of family members with mitochondrial disease, or mtDNA mutations, as being his mother, a sister who died at three days old, three other sisters and their children. This submitter likened mitochondrial donation as a 'chance to break this cycle of generation after generation of health catastrophes in families like mine'.[32]

2.30 Other submitters described the 'dashed hopes, heartbreak and utter despair' of being a parent to a child with mitochondrial disease:

> Our oldest son…presented in 1980 at the age of four with intermittent rhythmic convulsions of his right hand. These became progressively more frequent and more violent until he died three years later.
>
> When a precious seven-year-old son, his frail body wracked by convulsions, asks if he's going to die what does one say? [He] knew, and

28 Name Withheld, *Submission 18*, p. 1.

29 Name Withheld, *Submission 18*, p. 1.

30 Name Withheld, *Submission 9*, p. 1.

31 Name Withheld, *Submission 36*, p. 1.

32 Name Withheld, *Submission 36*, pp. 1–2.

> told us what he wanted to do before he died - another visit to the Snake Hut at Taronga Zoo, a special cake for afternoon tea and much more.[33]

2.31 A submitter described the impact of mitochondrial disease on her son, diagnosed at age 22:

> He is now age 40 years and the disease is slowly affecting his ability to cope with everyday living. At age 22 when he was first diagnosed with the disease he had a double chamber pace maker fitted to his heart. Since then the disease has been gradually affecting his health in areas such as hearing and eye sight. He now requires hearing aids and regular eye testing. He is at the stage where he has very poor vision in one eye and needs glasses to help with his sight. It is affecting his balance and he is reluctant to negotiate stairways etc. He has also been told he is on the verge of being affected with diabetes but is trying to avoid it with healthy diet and exercise. All brought about by mitochondrial disease. Although he tries to stay positive I can see at times that he has his down moments trying to cope with daily life. Unfortunately there is no known cure for this disease and no way of knowing what further health implications may arise for him in the future.[34]

2.32 Shelley told the committee of her brother's condition, which affected his energy:

> It was something that I didn't consider in terms of energy. Energy is also about swallowing. It's about having the energy to swallow. It's about having the energy to breathe, because all of those muscles are affected, and all of that energy is used. Your brain uses 20 per cent of your energy, so you're using so much of that energy every day to do things. So he struggled to eat. He struggled to put on weight. He struggled to keep that energy maintained. With the myoclonus seizures and the hearing loss, he then started experiencing vomiting. He would experience severe headaches. He was then investigated a bit further, and he was then given a diagnosis of stroke-like episodes, where he would suddenly lose strength in one side. But these sorts of strokes are more metabolic crises. It's that energy that you lose in your brain, which resulted in hallucinations. He started seeing little people on the floor. It also resulted in him not being able to communicate, because he had words in his head that he couldn't get out.[35]

2.33 Justin told the committee of the impact that losing his sight, as result of mitochondrial disease, had on his life: 'As you can imagine, when you lose your sight in the middle of your life it can have a devastating effect on your psychology, on your way forward and on your life generally. I am a single man and live alone, and so my independence has paid a price for that'.[36]

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33 Name Withheld, *Submission 14*, p. 1.

34 Name Withheld, *Submission 11*, p. 1.

35 Shelley, *Committee Hansard*, 17 May 2018, pp. 33–34.

36 Justin, *Committee Hansard*, 17 May 2018, p. 35.

Impact to families

2.34 Submitters and witnesses described the devastating effects of mitochondrial disease, both on the impacted individual and on their families. Ms Monica Ferrie, Chief Executive Officer of the Genetic Support Network of Victoria described the 'suffering' of Australian families:

> Children are being born with preventable disease and people are living with diseases that would be preventable through mitochondrial donation. Mothers pass this mitochondrial DNA onto their children and sometimes they can suffer as a result of knowing that their DNA has passed the disease on to their children.[37]

2.35 A submitter with three children affected by mitochondrial disease described the impact to her family:

> The personal, emotional, social and financial impact of the illness within our family, the loss of a daughter at age 18 after a 10yr battle, the decline in our 17yr old son who is potentially repeating the same battle again, and to look into the eyes of our 12yr old daughter who wonders if she is next and not wanting a child of her own dying the same way, is an impact I even find hard to imagine and repeatedly pinch myself, hoping to awake from this 'dream'.[38]

2.36 Another woman with mitochondrial disease submitted that her diagnosis directly impacted her decisions whether to have children:

> During my pregnancy I had no idea that my condition could be genetic and could affect my child, who is now 21yrs. Upon realising the then [sic] possibility of genetic implications, I made the sad decision that I would not risk passing mitochondrial disease onto any of my future children [and] that I would not have any more children. When he was younger, my son David would ask if he could have a sibling, unfortunately he grew up as an only child [and] we do not yet know if he will become affected by mitochondrial disease as I still have not yet received a genetic diagnosis.[39]

2.37 Mary told the committee of the significant impact that mitochondrial disease had in her family, which included 19 people with mitochondrial disease. 'I am in a position where I have the disease. I look after children who have the disease, and I'm also a carer for my mother who has mitochondrial disease. It really has devastated every generation of our family'.[40] Mary went on to state that in her family, mitochondrial disease was also characterised by stillbirth and late miscarriage, and

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37 Ms Monica Mary Ferrie, Chief Executive Officer, Genetic Support Network of Victoria, *Committee Hansard*, 17 May 2018, p. 2.

38 Name Withheld, *Submission 18*, p. 2.

39 Name Withheld, *Submission 33*, p. 2.

40 Mary, *Committee Hansard*, 17 May 2018, p. 34.

more broadly mitochondrial issues have a strong association with autism and other complications.[41]

Costs of mitochondrial disease

2.38 There are many costs for people living with mitochondrial disease, both to the healthcare and social services systems, as well as significant out of pockets costs to individuals. There are also related costs that are more difficult to quantify, such as carer costs of reduced economic participation.

Healthcare costs

2.39 AMDF provided an estimate of lifetime health care costs for a child born with a rare disease at around A$2.5 million in the UK and about A$5 million in the United States of America (USA).[42]

2.40 Other submitters also pointed to the very high costs of medical care for babies with severe mitochondrial disease. One submitter, the grandparent of a baby who lived only a few months, provided an estimation of medical costs:

> On top of the very sad personal and social costs of this trauma, the economic costs to the national healthcare budget of M's short life were significant and should be noted. Based on the 2013 schedule of fees for non-eligible (foreign visitor) patients for Eastern Health (BHH), it has been estimated that over M's life, true (not out-of-pocket) costs might have amounted to $300–350 thousand dollars. …
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> If M had had a less severe version of mitochondrial disease and lived longer, the public costs via [the National Disability Insurance Scheme] and other schemes of assistance would have been much greater.[43]

2.41 One submitter outlined the varied medical costs as including 'constant visits to endocrinologists, cardiologists, neurologists, physiotherapists, psychologists and other professionals, as well as medication and transport costs etc'.[44] The submitter went on to cite the introduction of the National Disability Insurance Scheme (NDIS) as an opportunity to coordinate services for people, but stated that because mitochondrial disease often takes years to diagnose, there will still be a strain on the medical system for many more years than necessary.[45]

2.42 AMDF also noted the NDIS as an improvement to the lives of some families living with mitochondrial disease, citing information gathered from members of the mitochondrial disease community that prior to the NDIS, families were paying thousands of dollars out of pocket for medical and therapy costs. AMDF estimated

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41 Mary, *Committee Hansard*, 17 May 2018, pp. 34–35.

42 AMDF, *Submission 26*, p. 12.

43 Name Withheld, *Submission 39*, p. 2.

44 Name Withheld, *Submission 8*, p. 2.

45 Name Withheld, *Submission 8*, p. 2.

that the cost to taxpayers via the NDIS could range up to $120 000 per month for one individual child with mitochondrial disease.[46]

2.43 One submitter with mitochondrial disease outlined an estimate of costs for their case of adult mitochondrial disease:

> The amount I have used the Medicare system and gone beyond my threshold in the last 2 years is unbelievable. In 2016 alone Medicare had to pay for approximately $4000 worth of testing and Medical Professionals Fees. So for myself alone without adding up all of what other mitochondrial Disease patients use, it is taking a lot out of the system and if this can be prohibited for future generations, I believe this is our best option.[47]

2.44 Justin also pointed to the high health care costs of mitochondrial disease and told the committee that even with his diagnosis, which he described as relatively straightforward, his testing included 'two MRIs, lots of blood and urine tests, audiology testing, cardiology testing, gene testing and visual exams, all funded by the public purse'.[48] Justin went on to say his ongoing care included seeing 'many different specialists in Adelaide, where I live, and also here in Sydney. I see four different specialists here, including Professor Sue. It's also funded by Medicare, of course. I also have a heavy reliance on my GP, of course'.[49]

2.45 An economic analysis of the health system and administrative costs of introducing mitochondrial donation undertaken by the Health Department in the UK calculated a net benefit of GBP32 million per annum (approximately A$61 million) for mitochondrial donation if it enabled the births of just 20 healthy children per year.[50]

2.46 That estimate does not include savings from social services, income support or the increase in economic participation of affected individuals, parents and other carers. Other health cost information from submitters shows that in the USA, direct costs for hospitalisation of mitochondrial disease patients is approximately US$113 million per annum.[51]

2.47 Professor Thorburn provided an estimated health care savings of A$33 million to A$66 million per year from introducing mitochondrial donation in Australia, resulting in a conservative estimate of five to 10 children born without mitochondrial disease.[52]

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46 AMDF, *Submission 26*, p. 12.

47 Name Withheld, *Submission 32*, p. 2.

48 Justin, Committee Hansard, 17 May 2018, p. 36.

49 Justin, *Committee Hansard*, 17 May 2018, p. 36.

50 Professors Thorburn, Christodoulou, Sue, Carroll, Ryan and Filipovska, *Submission 59*, p. 4.

51 Associate Professors Catherine Mills and Karinne Ludlow, Professor Robert Sparrow, Dr Narelle Warren, *Submission 20*, p. [11].

52 Murdoch Children's Research Institute and Victorian Clinical Genetics Services, *Submission 23*, p. 16.

Other costs

2.48 Submitters described the cost of mitochondrial disease as being much broader than the medical costs, as people with the disease – and their carers – have significant loss of economic activity:

> She was unable to work, drive a car or socialize. Eventually she lost all independence and could not cook or care for herself. One of us, usually her mother, had to be with her constantly.[53]

2.49 A young woman with mitochondrial disease submitted that she often relied on family assistance for daily activities. She submitted 'I become reliant off their assistance for the things that I can no longer do myself. They help me cook, shower, drive, and constantly support me through my darkest of times'.[54]

2.50 The parents of a young boy with mitochondrial disease outlined the costs of mitochondrial disease as being threefold. Firstly there were medical and support costs of medical specialists, classroom supports, subsidised medicine, weekly therapy sessions and an assumed lifetime of welfare dependency. Secondly, the parents had an economic participation cost, as both had worked part-time since their child's diagnosis and it was expected at least one parent would have to quit working to become a full time carer. Thirdly, the parents pointed to the emotional cost, saying '[t]he emotional drain on our lives, the lives of our families and friends have been significant, this has impacted our sense of wellbeing and happiness in society'.[55]

2.51 Justin told the committee that due to his vision loss from mitochondrial disease, he received a blind pension, as did his sister: 'I also receive a mobility allowance and transport concessions that are very useful but are, of course, a drain on the public purse. Likewise, my return to work has been facilitated by very expensive technology that allows us to adapt our workplace through software and other modifications. I would estimate, from what I understand, $25 000 to $30 000 has been spent on that alone. That process has been assisted by the support of a disability support organisation, also funded by the public purse.' Justin also pointed to the impact to his economic activity, as he formally had a senior role in the South Australian Government and now had a part-time role in a less senior position.[56]

2.52 Professor Aleksandra Filipovska, an expert in mitochondrial disease with the Harry Perkins Institute of Medical Research, outlined the varied costs of mitochondrial disease and their impact to individuals and families:

> Because of the severe and drawn-out course of these diseases, the emotional, societal, and financial costs are devastating. As a researcher who has had experience in providing molecular diagnosis for patients and families affected by mitochondrial disease I have seen the devastation it

53 Name Withheld, *Submission 14*, p. 2.

54 Name Withheld, *Submission 32*, p. 2.

55 Name Withheld, *Submission 38*, p. 2.

56 Justin, *Committee Hansard*, 17 May 2018, p. 36.

> causes not just in terms of the difficult pathologies but the stress and emotional turmoil in caring for the affected loved ones as well as the concerns related to future family planning.[57]

Options for having children

2.53 A diagnosis of mtDNA mutations, whether or not it has manifested itself into mitochondrial disease, has strong implications for the ability to have healthy children because the mutations are inheritable. Professor Thorburn noted that, in some cases there is a 100 per cent chance of passing on the mtDNA mutation.

2.54 A submitter affected by mitochondrial disease considered its heritability to be one of the worst aspects of the disease:

> The trauma of watching both my mum and brother deteriorate so rapidly and so devastatingly, will stay with me forever…Knowing all this, and losing half my family in 16 months is difficult. What makes it even more life changing is finding out that I too have this disease and will possibly face the same devastating journey. But worse than this, I would almost certainly pass this disease on to my children.[58]

2.55 A submitter described the option of having children without intervention as a gamble:

> [I]f you have a defect in your mitochondrial DNA, you're essentially making a gamble. There's no way of knowing if you'll pass on a little bit of the defected mitochondria or all of your defected mitochondria. Meaning the child could have a mild to extreme form of the illness. Mild like me or extreme and be terminal. And we're just not the gambling types.
>
> However, the introduction mitochondrial donation IVF, literally removes the risk of throwing the dice and gambling with a future child's health.[59]

2.56 Another submitter described mitochondrial disease as a 'ticking time bomb' hanging over multiple generations of their family.[60]

2.57 One submitter, a parent of a young child with mitochondrial disease, described the situation faced by people with mitochondrial disease when considering having children:

> Families with Mitochondrial disease face a terrible choice. Do they run the risk of passing their mitochondrial donation onto the next generation or lose the opportunity to have children?[61]

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57 Professor Filipovska, *Submission 17*, p. 1.

58 Name Withheld, *Submission 8*, p. 1.

59 Name Withheld, *Submission 9*, p. 1.

60 Name Withheld, *Submission 39*, p. 2.

61 Name Withheld, *Submission 38*, p. 2.

2.58 Shelley told the committee about the increased importance of having a child with a genetic link to couples who faced the potential of one of them dying early from mitochondrial disease:

> We're not going to play god. We don't want to design a baby. We just want to have a healthy child as much as possible and be able to call them our own. If something were to happen to me, which I believe it will, my husband can look at that child and say: "You've got your mum's eyes. You've got her personality. You've got her smile. You're just as kind as she was." So, for us, that's a really important component that we believe this can offer us.[62]

2.59 The current options available to women with mtDNA mutations when considering having children are primarily to use donated eggs or to adopt.

2.60 For women who want to have a child with a genetic link, an option is in vitro fertilisation (IVF) using pre-implantation genetic diagnosis (PGD), where embryos are tested before implantation to look for those with the lowest proportion of mutated mtDNA. This option only works for some types of mitochondrial disease and has other limitations.

2.61 The various options for having children with a reduced risk of mitochondrial disease are outlined below.

IVF and Pre-implantation genetic diagnosis (PGD)

2.62 As discussed above, PGD is an IVF technique used to test the embryo prior to implantation. A key limitation to this method is it cannot be used by all women with mtDNA mutations. Some women have normal and mutated mtDNA in their cells (heteroplasmy) and others have all mutated mtDNA (homoplasmy). PGD can only benefit women who are heteroplasmic. Moreover, this technique can only reduce, not eliminate the risk of having an affected baby. Even if unaffected themselves, girls born after the use of this procedure may themselves still be at risk of having affected children, as some abnormal mitochondria may be present in their eggs.[63]

2.63 A group of leading scientists in the field of mitochondrial disease submitted that women with lower amounts of mtDNA mutations are at lower risk of having a child affected by mitochondrial disease and techniques such as PGD can be appropriate.[64] However, the submission goes on to state:

> [I]t remains impractical to predict the actual risk for most women, many of whom are thought to have a risk of between 50% to 100% of having a child with severe disease. Thus for probably most women from families with

62 Shelley, *Committee Hansard*, 17 May 2018, p. 34.

63 House of Commons Library (UK), *Mitochondrial Donation*, Standard Note: SN/SC/6833, 29 January 2015, pp. 6–7.

64 Professors Thorburn, Christodoulou, Sue, Carroll, Ryan and Filipovska, *Submission 59*, p. 1.

> mtDNA disease, mitochondrial donation offers the best prospect of having a healthy child related to both parents.[65]

Prenatal diagnosis

2.64 Prenatal diagnosis can be conducted on a pregnant woman at around 11–14 weeks gestation, usually by performing a genetic test on a placental tissue biopsy. If an mtDNA mutation is found, parents then face a choice of either continuing or terminating the pregnancy.[66]

2.65 Professor Christodoulou explained the improvements in prenatal testing in determining potential genetic mutations in a foetus:

> [D]epending on which specific mitochondrial DNA change you're looking at, you can actually be very accurate in your prediction about what the likely outcome of that will be to subsequent babies…for instance, for a particular mitochondrial DNA mutation, pre-implantation genetic diagnosis is a very viable alternative to mitochondrial donation. However, for many other mitochondrial DNA mutations, mitochondrial donation is really the only option.[67]

2.66 Professor Thorburn further told the committee that for some women, a low mtDNA mutation load means they have a low risk of passing on mtDNA mutations to children and prenatal diagnosis and PGD are good options, however 'for the majority of women, there is going to be a substantial amount of the mutant mitochondrial DNA in many or all of their eggs and so it's very unlikely that those techniques will work. It's quite complicated genetics'.[68]

2.67 A submitter affected by mitochondrial disease explained the PGD process she had undertaken. She had undertaken five IVF cycles – at a cost of $7000 per cycle – which retrieved around 50 eggs, from which only two embryos had a relatively low mutation loading of 32 per cent, not meeting the generally accepted benchmark of a maximum 15 per cent mutation load:

> Emotionally, the rollercoaster of having to desperately rely on success at each stage – retrieving as many eggs as possible, having them fertilise, seeing how many survive and grow to day 5, then biopsy the surviving embryos to establish their mutation loading. Going through each stage of a cycle generally means going from 14 eggs down to 3 biopsied embryos only to find out that they do not meet the loading threshold. It is a difficult and draining process that seems unfair and frustrating. With any couple

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65 Professors Thorburn, Christodoulou, Sue, Carroll, Ryan and Filipovska, *Submission 59*, pp. 1–2.

66 Mitochondrial Disease News, *Prenatal Diagnostic Testing for Mitochondrial Diseases May Help Future Parents, UK Study Shows*, 10 March 2015, https://mitochondrialdiseasenews.com/2015/03/10/prenatal-diagnostic-testing-for-mitochondrial-diseases-may-help-future-parents-a-study-in-uk-shows/ (accessed 15 June 2018).

67 Professor Christodoulou, *Committee Hansard*, 17 May 2018, p. 16.

68 Professor Thorburn, *Committee Hansard*, 17 May 2018, pp. 15–16.

> trying to have a child, time is a factor, as well as health. For us, PGD seems to show little success.[69]

2.68 Another submitter described the PGD process that her daughter had undertaken, after losing a baby to mitochondrial disease. The daughter had undergone a year of IVF with PGD and had embryos implanted, but had no success through IVF. The submitter argued that they considered the best option for their family was one that was not open to them because mitochondrial donation is prohibited by legislation.[70]

2.69 Mary described her experiences with IVF and genetic counselling as a 'process of discussing the value of our unborn children's lives'. Mary further told the committee that:

> Mitochondrial donation gives my children a chance to not go through that, to not have to consider the value of their own lives and those of their unborn children, and to raise healthy children who, in turn, will then have healthy children. If we choose not to do this there is no choice for our family. There will just be generation after generation of this terrible disease.[71]

Non-genetic options: adoption, fostering or donated eggs

2.70 Submitters who were not in favour of mitochondrial donation, generally for ethical reasons, argued that other options could be used for people with mtDNA mutations who wished to have children. These were primarily adoption or fostering, or the use of donor eggs for IVF.

Donor eggs

2.71 Another option that was suggested as a possible alternative to mitochondrial donation was using IVF in conjunction with an egg donated from an unaffected woman.

2.72 As outlined by Professor Sheryl de Lacey from Flinders University, most egg donation in Australia relies on local donors who are often family members. Egg donation from family members is obviously not suitable for mitochondrial disease which is a genetic condition. An estimated 25 per cent of Australian patients who cannot get a local donor acquire one from overseas. This raises its own ethical challenges due to differing regulation of the donor process and information in those jurisdictions.[72]

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69 Name Withheld, *Submission 8*, pp. 1–2.

70 Name Withheld, *Submission 39*, p. 2.

71 Mary, *Committee Hansard*, 17 May 2018, p. 35.

72 Professor Sheryl de Lacey, *Submission 55*, p. 3.

Adoption and fostering

2.73 Critics of mitochondrial donation argued that adoption or fostering 'would offer a simpler path'[73] to parenthood. However, adoption and fostering programs in Australia have strict eligibility criteria, including health screening. AMDF has sought information on eligibility for people with mitochondrial disease (or asymptomatic mtDNA mutations) and in a submission indicates a lack of definitive advice on eligibility. AMDF notes that this is generally due to a lack of specific preclusions.[74]

2.74 AMDF further notes in a submission that given the level of trauma that children involved in adoption have faced, states and territories 'have a preference towards prospective parents who have the highest possibility of seeing children into adulthood'.[75]

2.75 Anglicare is an Anglican diocese-run charitable organisation that offers foster care and adoption services. On its website, Anglicare lists its eligibility criteria for families looking to adopt. One of the criterion relates to health which relevantly provides:

> Health – Applicants must be non-smokers, in good general health with normal life expectancy.[76]

2.76 Even if people living with mitochondrial disease were eligible to adopt, Professor de Lacey explained that adoption is not a simple substitute for biological reproduction. In Australia, there are few children in need of adoption and most children are adopted by people who already care for them.[77]

2.77 Professor de Lacey provided the committee with the statistics on local Australian adoptions in 2016–17:

> Of the total number of adoptions only 42 (13%) were 'local' adoptions, ie. Adoptions of an Australian child to parents not previously known to them.

2.78 While it might entail less scientific risk than mitochondrial donation, it is not clear that adoption is necessarily an option for women living with a mitochondrial disease.

2.79 For some submitters, adoption or fostering was not considered a suitable option, as they had a strong desire to have a genetically linked child:

> We have considered all the other avenues of egg donor, adoption or not having children. We have a strong desire to have our own child who

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73 Australian Catholic Bishops Conference, *Submission 28*, p. 2. See also Australian Christian Lobby, *Submission 51*, p. 8; Social Issues Committee of the Anglican Church Diocese of Sydney, *Submission 56*, p. 3.

74 AMDF, *Submission 26.1*, [p. 13].

75 AMDF, *Submission 26.1*, [p. 13].

76 Anglicare, *Looking to Adopt*, https://www.anglicare.org.au/what-we-offer/foster-care-adoption/adoption/looking-to-adopt/ (accessed 30 May 2018).

77 Professor de Lacey, *Submission 55*, p. 3.

> inherits our genes, our personalities, ourselves. If something were to happen to either of us, we would still have a part of each other. When we heard about mitochondrial donation, we felt that this would provide us with the opportunity to have a child who would be genetically (99%) ours, but most importantly healthy.[78]

Remaining childless

2.80 Critics of mitochondrial donation have also proposed the option for remaining childless should be considered by people with a risk of passing on mitochondrial disease. Archbishop Anthony Fisher, Archbishop of Sydney and Vice Chair of the Australian Catholic Bishops Commission, told the committee that 'obviously the more serious the risk [of passing on mitochondrial disease] the more you are going to have to think very carefully and act responsibly'.[79]

2.81 The submission from the Anglican Church Diocese of Sydney states:

> [W]e do not believe that a 'right' to a biological child exists, and can see no grounds by which such a right would be established.
>
> We therefore do not accept the premise that any means available to obtain offspring should be made available to individuals suffering from the inability to ensure that their offspring is healthy.[80]

Committee view

2.82 The committee notes that for many people there is a desire to have a genetically linked child.

2.83 The committee also notes that reproductive technology is widely used by the Australian community, including the use of donor gametes. Donor gametes are commonly used to overcome medical infertility, social infertility or transferable genetic conditions. As a result many families are successfully created where the resulting offspring is not genetically linked to one or both parents.

2.84 The committee notes that reproductive technology is expensive for both taxpayers and prospective parents. The committee considers that it is desirable for governments to support fertility treatment as a social good. However, it does not support the notion that the state has an unlimited responsibility to support people to become parents, and considers that any such treatments should be provided on an equitable basis.

Mitochondrial donation

2.85 As outlined in chapter one, mitochondrial donation is a technique to replace the mutated mtDNA in an egg, or a pre-embryonic fertilised egg. Chapter three discusses the science in greater detail.

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78 Name Withheld, *Submission 8*, p. 2.

79 Archbishop Anthony Fisher, Vice President, Australian Catholic Bishops Conference, *Committee Hansard*, 17 May 2018, p. 68.

80 Social Issues Committee of the Anglican Church Diocese of Sydney, *Submission 56*, p. 1.

2.86 A number of witnesses and submitters impacted by mitochondrial disease made strong requests for this technology to be made available to Australian families. A submitter who had two children die from mitochondrial disease described mitochondrial donation as an opportunity for future children to 'experience the joys and sorrows of a full life that [their children] couldn't'.[81] The submitter went on to state:

> Our remaining children have had their DNA sequenced and they know they won't develop mitochondrial disease so in that sense the uncertainty for our family is over. But for other families with mito around Australia who want to have children, their nightmare is only beginning. The constant anxiety and sense of hopeless foreboding at knowing that their precious child could be affected is overwhelming.[82]

2.87 Another submitter argued that as there is no cure for mitochondrial disease, mitochondrial donation is the only hope for some families:

> A big black cloud that has been hanging over my family for years is slowly starting to dissipate. If this technology was available when I was having my children, I most certainly would have used it and I will be strongly encouraging my daughters… to consider Mitochondrial Donation if ever they decide to start a family.[83]

2.88 Professor Sue, a clinician working in mitochondrial disease, told the committee of that she sees patients on a weekly basis who are asking for access to this technology 'because the patients are traumatised by family members being lost, they live day to day with the burden of illness of this disorder and they are keen to have children without this disorder.'[84]

2.89 Another submitter put their request very simply:

> Please approve [mitochondrial donation]…no Mother should have to sit by a bed watching their children die of something that you have in your power to help prevent.[85]

Committee view

2.90 The committee agrees that mitochondrial disease is a devastating and often life-threatening condition. The traumatic impact to parents who have watched their child die, in some cases more than one child, cannot be overstated.

2.91 The committee further agrees that there is a desire in most people to have a genetically linked child.

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81 Name Withheld, Submission 14, [p. 2].

82 Name Withheld, *Submission 14*, [p. 2].

83 Name Withheld, *Submission 15*, p. 2.

84 Professor Sue, *Committee Hansard*, 17 May 2018, p. 24.

85 Name Withheld, *Submission 6*, p. 1.

2.92 There are a range of options for people impacted by this genetic condition to have children. However, many of those options do not result in a genetically linked child and others are not suitable for women with certain mtDNA mutations. For those women, and indeed the children they wish to bring safely into this world, mitochondrial donation may provide a new option.

2.93 The committee is cognisant that this technology, like all new medical therapies, comes with risk and ethical concerns that must be taken into consideration prior to any possible change in legislation.