Oxford Mitochondrial Patient Information Event – Q&A session
Friday 30th April 7pm

Q: Is there a central database for Mito where researchers can access info on different Mito patients?

A: Yes! We have a national database sponsored by the Wellcome Trust, held securely at Newcastle University, call the 'MitoCohort'. This database serves as a way of looking at the natural history of mitochondrial disease in a large group of confirmed patients in the UK. It also serves as a useful resource in order to readily identify groups of patients that may be suitable for clinical trials. Anyone with a genetic or biochemically confirmed mitochondrial disease is welcome to be part of the cohort study. No additional appointments or investigations are necessary and your data is anonymised. You may not be offered the opportunity to take part in a clinical trial and are not obliged to take part if you were offered a research study opportunity.

All 3 mitochondrial centres are also working together with researchers at Oxford University to develop a patient registry known as the RUDY study. Funded by The Lily Foundation, this database will allow patients to enter their own data and provide more regular updates on their condition. There will be the opportunity to complete questionnaires to gain a real insight into how mitochondrial disease affects you.

Contact your Mitochondrial Centre, or research nurse, for further information on both studies.

Dr Victoria Nesbitt, Clinical Lead

Q: ***I am told my mito is maternally inherited, so presumably, comes through my nan and her mother's (my great grandmother) genes? My Nan was one of 12, including 6 girls, one died at birth but the others, aside from migraines, Alzheimer's, Parkinson's, various cancers and IBS, they, nor their children/ grandchildren show signs of carrying the gene. My brother died at 19 months to a neurological condition (presumed Leigh's, but he had no formal testing as died before, so Drs guessed from a MRI). Why, in such a huge family is it just me and my brother who got the bad mito gene? It doesn't make sense! I feel like because I am the only obviously disabled young person I don't fit in and am never included. Why was it just me born like this? How come its just 2 out of many?***

A: It is important to acknowledge that having a genetic condition can understandably raise difficult feelings, and it is very common to ask 'why me?' when you are diagnosed with a genetic condition like a mitochondrial disease. Genetic conditions can be random and they can happen to anyone.

So why do mitochondrial conditions sometimes only affect one or two family members?

The short answer is chance. Just because a condition is genetic it doesn't always mean that condition is passed on in a family.

But the chances will be different depending on which gene is involved and how the alteration in that gene is passed on (i.e. which *inheritance pattern* is involved). For maternally inherited mitochondrial conditions the chance of having symptoms also depends of the level of damaged mitochondrial DNA you may have. The level of damaged mitochondrial DNA that someone may inherit is random and can vary from person to person in the same family. In general, some family members may inherit a low level of damaged mitochondrial DNA but not experience problems. Others may inherit a higher level and have symptoms. For a more detailed, personalised answer and understanding of how your mitochondrial condition has happened, and what this might mean for you and others in your family, we would recommend speaking to your mitochondrial specialist or genetic counsellor.

Jo Lowndes, Principal Genetic Counsellor

Q: ***Why have I been asked to have a second biopsy? I've been told that my genetics are all normal.***

A: This would depend on the specific circumstances of the situation but some general points are that normal genetics does not exclude a diagnosis of mitochondrial disease as not all genetic causes are known or possible to detect with current testing methods. Scientific knowledge and lab technologies are continually expanding and developing. Genetic testing is typically targeted to specific genes or panels of genes based on other evidence including muscle biopsy findings. This is to focus on the genes that we currently know how to interpret or the genes that we think are the most relevant for the clinical symptoms and results of other investigations. Therefore, different patients may have had different genetic tests and another biopsy may help direct further genetic testing.

Also, the need for a second biopsy will depend on results of the previous biopsy, how long ago this was, and how clinical symptoms have changed since then. The types of investigations done on muscle biopsies may give more variable results than the genetic tests done on blood samples. They are often measurements of things which may change over time with disease or with normal aging, both in development as a child or aging as an adult, such as the amount of mitochondrial DNA or looking at the appearance of the muscle fibres down a microscope. Therefore the first biopsy may have given inconclusive results and a repeat biopsy may help provide additional support for a diagnosis or alternatively may help confirm that the previous results were normal. A second biopsy may also provide information on disease progression, for example whether things have changed over time or stayed the same.

Kate Sergeant, Principal Clinical Scientist

Q: ***Fatigue is a big problem for me. I take CoQ10 which helps (I think!) but some days I struggle to do anything.***

A: Fatigue is experienced by many people with a variety of medical conditions and is therefore not exclusive to mitochondrial disease. However it is understandable in mitochondrial diseases because we know that the mitochondria are responsible for generating the energy in the cells. Mitochondria are like batteries and are prone to run down so a bit like your mobile phone or laptop the performance slows down when the batteries are low or the system is overloaded.

There are no magic solutions to fatigue but we do know that regular meals, a healthy diet, regular routine; including exercise and good sleep hygiene are all important and have a role to play in fatigue management. Co Enzyme Q10 can assist as it helps with energy transport but it can't solve the issue completely.

We often talk about pacing as a strategy to manage fatigue, this means trying to avoid the pitfall of 'boom and bust' i.e. over doing things one day and paying for it for the next 2-3 days. This is not as easy as it sounds and requires discipline. That said apart from being very frustrating and interfering with everyday life overdoing things, within reason, is not dangerous.

Counter intuitively taking regular exercise can help with fatigue symptoms because exercise boosts energy levels and improves circulation and oxygen transport. Short bursts of exercise should be part or a daily routine or weekly programme. There is some evidence to suggest that 5-10 minutes of brisk walking or energetic activity might be better than a 30 minute slower walk where fatig8e is an issue.

We have a fact sheet on the website and can offer specific 1:1 advice when people come to clinic or over the phone.

Jane Freebody, Specialist Physiotherapist

Q: What exactly is a stroke like episode? What is the difference between a stroke like episode and PRES?

A: stroke-like episode is an evolving neurological event occurring at any age, driven by underlying seizure activity (even if you have no known history of seizures). It is most commonly associated with m.3243A>G and POLG. It is different to a 'vascular stroke' which is usually confined to a specific area within the brain supplied by certain blood vessels. On a brain scan (MRI) we can usually tell if it has been a vascular stroke or a metabolic stroke (stroke-like episode) because of the areas of the brain affected. PRES is posterior reversible encephalopathy syndrome. It may present in a similar way to a stroke-like episode – headache, seizure, encephalopathy, visual disturbance, confusion but the changes on MRI are seen at the back and sides of the white matter of the brain. Usually patients affected by PRES recover (as can patients with stroke-like episodes) and the changes on MRI resolve (which does not usually happen in stroke-like episodes).

Dr Victoria Nesbitt, Clinical Lead

Q: ***We're told to eat lots of carbohydrates often, but then I put on weight because of the exercise intolerance and pancreatitis and then I'm in trouble for that, so how can we be expected to do all of this?***

A: I do empathise with your complex issues. Regular small meals and snacks containing carbohydrate is an important message. If you have problems with excess weight gain then you can look at reducing fats in your diet. Always choose low fat foods especially margarine, yoghurts, and milk. If you go around the supermarket and look at the fat content per 100g of foods, make sure you are choosing the lowest. Don't add extra oils; grill foods; cut the fat off meat. Maybe ask the physios for some advice about doing some exercises that you can manage without becoming too fatigued.

Judy Wadsworth, Paediatric Metabolic Dietician

Q: ***I find it difficult to swallow bread and to chew meat. Is there anything I can do to make it easier or should I just avoid eating them?***

A: Bread and meat are both quite dense textures which can take more energy & repetitive muscle movements to chew, which can be more difficult for those patients who struggle with muscle weakness and fatigue. I would suggest trialling softer bread with moist fillings such as tuna mayonnaise, egg mixed with salad cream/mayonnaise. With meat I would suggest using it in casseroles or slow cooked meals so that it easily falls apart when pressed with a fork. Making the meat more moist with the addition of gravy or sauces can also help to make it easier to chew too. If you are still finding soft chew consistencies difficult to manage then we can discuss a 'Minced and Moist' diet.

Claire Blair, Highly Specialist SLT

Q*: I have lost confidence to walk outside without someone with me as find the change in ground surface can make me wobbly. Is there anything I can do or is it just my disease progressing?*

A: Yes there is something that you can do and no it isn't necessarily disease progression. Most patients progress slowly unless they have other health issues that affect their Mitochondrial disease. It is important where possible to undergo a baseline physiotherapist if possible with your Mitochondrial Specialist physiotherapist or a neurological/balance physiotherapist. You need to know what parts of your balance system are working and what isn't tip top! Physiotherapists can give you a home exercise programme

INSIDE: Start small to be confident outside you need to be able inside first

Standing still/practising different movements

Gradually increase the time or distance as able

Walking on a flat surface (Libraries /supermarket) next to a wall where you can prop and gradually make your hand a lighter prop until you have just light fingers and then walk without

You will know then whether you need an outdoor prop

OUTDOORS:

Stepping in and out of the front door
Flat surface you may need taking to a flat walkway (tarmac/concrete)
Hiking poles make great props as they give you extra feedback through your arms from the walking surface and correct your balance
Outdoor walkers come in fun colours and can be lightweight
They are a mobile prop and mean that you are in charge. They often have a little seat for rests and most people will move out of your way so you don't have to mow them down!
If you enjoy outdoor activities there are specialist electric tricycles, disabled assisted charities (canoeing, sailing, gliding!) and also wheel chair ramblers.
Kate Browne, Vestibular / Balance Physiotherapist

Q: ***How do mito patients manage a good diet for if they have diabetes type 2 and who suffer from gastric issues as well?***
A: Management of type 2 diabetes would be to maintain a good healthy weight, avoid sugary foods and include starchy carbohydrate foods where the glucose is released slowly at meals and snacks (low glycaemic index). The idea is to achieve steady blood glucose levels throughout the day. Low GI foods include oats, pasta, basmati rice, seeded bread, fruit and pulses. Gastric issues can be quite varied but commonly this will be constipation. Treatment can include the use of Movicol (or similar medication). There is some research that a low fibre diet in adults might beneficial and so you could discuss this with a dietitian in your local community or contact your specialist Mitochondrial team.
Judy Wadsworth, Paediatric Metabolic Dietician

Q: ***Can someone please go over which antibiotics are safest for us and likewise, which general anaesthetic is safest as we all go through a lot of surgery and all get infections often.***
A: There are very few antibiotics / anti-microbials / anti-virals that are deemed not safe for patients with mitochondrial disease (linezolid, zidovudine; gentamicin if you harbour the m.1555G>A mutation). Ciprofloxacin and chloramphenicol should be used with caution but it is likely that you would become more unwell by not having these antibiotics if you needed them than if you had them! In terms of anaesthetics, we generally advise against prolonged use of propofol. As an initiative of the International Mitochondrial Patients (IMP), a group of experts in mitochondrial disease carried out a study into the safety of drugs in mitochondrial patients. The study took place on an international level and resulted in the publication of a list of drugs to be used with caution in primary mitochondrial disease. You can find an up to date list of medicines regarded as safe, and those to be used with caution, at https://www.mitopatients.org/mitodisease/list-of-medicines
Dr Victoria Nesbitt, Clinical Lead

Q: ***Why should we avoid random foods like mushrooms, and cheese with chives etc?***

A: I am not aware of the need to avoid any specific foods in Mitochondrial disease, nor were the rest of the team. I have contacted The Lily Foundation to see if they had heard any similar comments from other members, but they said that it hadn't been an issue that had been raised in any of their forums. My advice is therefore that you can eat those foods mentioned above, unless told not to for other reasons. We would always encourage a healthy balanced diet based on the Eatwell plate.
Judy Wadsworth, Paediatric Metabolic Dietician

Q: ***My 2 children have a rare genetic disorder SPATA5 which is believed to be a secondary problem rather than primary mitochondrial disease. What does this mean and should it still be treated as if it was a mitochondrial condition.***
A: Primary mitochondrial disease usually means that the cause originates in the genes that are involved in the function of the mitochondria, whereas secondary mitochondrial problems usually mean that the cause of the disease does not originate in the mitochondria but somewhere else in the cell and has a knock-on effect on the way that the mitochondria work. Since mitochondrial function is affected in these secondary diseases, often the clinical symptoms can be similar to those seen in mitochondrial disease. This may mean that treatment and management of the clinical symptoms may be similar for both mitochondrial disease patients and those with secondary mitochondrial problems. If not a true primary mitochondrial disease then treatment may be best managed by another more appropriate speciality. Also, until a genetic diagnosis is made it may be difficult to distinguish between primary and secondary and therefore many people with primary mitochondrial disease may be seen by different disease specialists and also people with secondary mitochondrial disease may be referred to a mitochondrial disease clinic for assessment and the results of subsequent investigations may find out that the disease is actually secondary. Sometimes even with a genetic diagnosis it may still be difficult to decide if the disease is primary or secondary, since it may be a new disease gene or a gene that we don't fully understand what its function is yet.
Kate Sergeant, Principal Clinical Scientist

Q: ***Is anyone going to liaise with all NHS hospitals in terms of emergency care as any time I'm admitted (despite my care plan) it's always a fight to be put on fluid though an IV. With chronic pancreatitis they never give me morphine fast enough because I'm 26 and they've never heard of mito and I'm left screaming because they think I'm a drug user.***
A: We're sorry to hear that this is the case for you. We are not able to liaise with all NHS hospitals in this way. We do, however, deliver education to hospitals across the country as far as we are able to, raising awareness as much as possible. In your own local hospitals, there will be staff turnover and the professionals on shift during your admissions will vary. The clinician will be assessing your immediate symptoms and needs and when they know that you have mitochondrial disease, they will bear this in mind. They do have to rule out anything unrelated to Mito that can be treated promptly. It would be too easy to point the

finger at your mitochondrial disease for every problem. However, this is where your emergency sheets are important and should be carried with you if you have to be seen by your local teams. The GP's or A&E doctors can use our contact details for further information. The Mito alert cards also have telephone and e mail contacts on them. We have got new ones printed up with our new clinic address and phone numbers. The Emergency sheets cover many aspects of problems that *may* occur. These sheets are generic and we do not wish you to think you would be likely to experience all the problems listed on them.

Sue West, Clinical Nurse Specialist

Q*: Is assisted dying is an option at all? Even if this means going to another country legally or doing legal paperwork.*

There are lots of considerations to be made here. We would advise that you speak to your Family Care Advisor and your family. Below are some resources that provide more information:

Advanced decisions
https://www.nhs.uk/conditions/end-of-life-care/advance-decision-to-refuse-treatment/
Making an advanced directive (includes a pack)
https://compassionindying.org.uk/making-decisions-and-planning-your-care/scotland/advance-directives/make-advance-directive/
Message in a bottle
https://lionsclubs.co/Public/messsage-in-a-bottle/
Power of attorney
https://www.gov.uk/power-of-attorney
Court of protection
https://www.gov.uk/courts-tribunals/court-of-protection
Dignitas
http://www.dignitas.ch/?lang=en

Heather Ryan, Family Care Advisor

Q: *What optic nerve research is being done to prevent blindness?*
&
Q: *Is research going into how eyesight can be prevented?*

A: Currently we no definitive treatment for inherited forms of optic nerve disease like those we see in mitochondrial disease e.g. LHON. Nonetheless there are some hopeful options on the horizon and being researched. Most notable is Idebenone – similar to Coenzyme Q10 – Idebenone has antioxidant properties and in clinical trials has been shown to improve visual acuity in some LHON patients. It is hoped that Idebenone may be able to be offered and trialled for other mitochondrial optic nerve conditions as well. The ultimate goal for treatment of any inherited eye disease however has to be the correction of the genetic

alteration that causes the condition, i.e. ***Gene Therapy.*** Gene Therapy Clinical Trials for LHON, where a working copy of the gene has been injected into eye, have shown some encouraging results and visual improvement for some patients. But further efficacy and safety studies are still needed. Similarly the promise for gene therapy treatments for inherited conditions that affect the retina is very optimistic, and it is hoped that with more research these advances can be translated to help mitochondrial patients with retinal disease.

Jo Lowndes, Principal Genetic Counsellor

Q: ***Can a mito patient donate blood or organs?***

A: Blood in circulation does not divide therefore mitochondrial mutations cannot be passed on by blood transfusion. However, you need to think about the affect that donating blood might have on you; your health comes first! The bone marrow makes blood cells, and this can be impaired in mitochondrial disease therefore it could take you a while to recover after donating blood. With regards to solid organ transplantation, in theory you can donate unaffected organs. However, those who have mitochondrial mutations that can cause multi-system disease could theoretically transfer an affected, but asymptomatic, organ to the recipient. The NHS transfusion service considers all requests on an individual case basis and if an organ from a mitochondrial patient became available this would be discussed with the transplant surgeon and recipient before deciding if the organ could be donated.

Dr Victoria Nesbitt, Clinical Lead

Q: ***I think I need to reduce my working hours but about worried about finances. What options do I have?***

A: It is difficult to say in general terms what your options would be because financial support is dependent on your income and the income of the people you live with, as well as any savings you have. The benefit that is designed to be an income for people who are unable to work due to a health condition is Employment and Support Allowance (ESA). To be eligible for ESA you must be working less than 16 hours and earning under £143 per week, and you must meet certain National Insurance conditions. For further details about these criteria and how much the ESA payments are, please see the gov.uk website: https://www.gov.uk/employment-support-allowance. Universal Credit could be an option if your income and savings fall below particular thresholds. If you have savings exceeding £16,000, you will not be eligible. However, the income thresholds are specific to individual circumstances, so I'm very happy to talk through these with patients on an individual basis. Please do get in contact with me directly if you would like to discuss this further. Alternatively, you could try using an online benefits calculator to see what you might be entitled to if your income changed. There is a useful benefits calculator available on the Turn2us website: https://benefits-calculator.turn2us.org.uk/AboutYou. However, please be aware that these calculators only provide estimates, and that not all benefits are included. If

you have any questions, you are very welcome to contact me or a benefits advisor at Citizens Advice.

Eliza Riley, Welfare Rights Officer

Q: ***Particularly for those of us without a named Mitochondrial disease but where one is clearly suspected, is there some way that Oxford could provide a co-ordinatory role?' Access to such records would need to be available to any doctor or professional involved in our care. Where, for example, a patient is seen by a number of different hospitals for various conditions like cardiac, diabetes, asthma, urology, thyroid disease, neurology etc, would it be possible to have all information about those clinics and results gathered together so that a full picture of that patient's health can be seen in context.***

A: The honest answer here is 'no' it is not possible to provide this type of role. Your GP is the key coordinating role in your care and should receive all the copies of referrals, clinics, follow ups etc. across the variety of disciplines if you have multi-system involvement. The problem we have is that we do not have access to all regional records available across the country from different teams and to coordinate, you would need this access. We are all on different electronic systems and we would not necessarily have automatic access just because we are clinical and/or Consultant led. Whilst in our care we would have access to local electronic records and if you are further afield, we ask that we be copied into any correspondence from wider teams so that we ourselves gather as much information as possible about you.

Sue West, Clinical Nurse Specialist

Q: ***Are there any plans for a Birmingham clinic? Oxford and London are my nearest but still 3 hours away each way and the journey is long for me. Or, will more appointments be vía webcam as this is very effective for me?***

A: NHS Highly Specialised Services have commissioned 3 centres in England to provide specialist care for patients with mitochondrial disease across the country, including Scotland and Northern Ireland, with additional referrals from Wales. Whilst we appreciate that many of our patients travel a long way to see us, we are unable to provide specialist services in additional areas at this time. We would advise that you make the most of your appointment and see all those members of the multi-disciplinary team that may be able to support your needs. If a physical examination is not necessary then a video consultation can be arranged.

Dr Victoria Nesbitt, Clinical Lead

Q: ***Is there any evidence of mito patients having problems with memory and forgetfulness?***

A: There are lots of reasons why a mito patient may have problems with their memory, or be described as being forgetful, which can include progression of their mitochondrial

disease. The brain requires a lot of energy and therefore is often affected by mitochondrial disease. Other factors that can impact on your memory include natural aging, infections, sleep deprivation and stress. Speak to your mitochondrial team if you are worried about your memory and further investigations, or assessments, can be arranged as deemed appropriate.

Dr Victoria Nesbitt, Clinical Lead