Oxford University Hospitals
NHS Foundation Trust

Oxford Rare Mitochondrial Disorders Service

Patient information evening Q+A

Can carriers of mitochondrial disease have symptoms of the disease?

This will depend on the mitochondrial gene alteration involved and how it is inherited. For example, for mitochondrial conditions caused by autosomal recessive gene alterations, such as TYMP (MNGIE), SURF1 (Leighs Disease) and DUUOK (mitochondrial DNA depletion syndrome) we would not expect carriers of these conditions to have mitochondrial symptoms, because carriers have one altered copy of the gene and one working copy; and one working copy of the gene is enough to keep someone fit and healthy. In autosomal recessive mitochondrial conditions both copies of the nuclear gene need to be altered and not working for someone to be affected by the condition.

In mitochondrial DNA (mtDNA) related conditions (for example mtDNA3243A>G which causes MIDD and MELAS) and autosomal dominant mitochondrial conditions (such as OPA1 which causes dominant optic atrophy) it is possible for someone to have or be described as a carrier of the gene alteration. However, whether the altered gene causes symptoms or not, and when those symptoms may appear and to what severity can be different in different people, even within the same family. These differences are probably due to other (as yet unknown) genetic factors.

I was told many years ago that not finding a genetic answer (a negative genetic test result) does not mean I don't have Mito, just that they haven't yet found the right gene alteration causing my condition. Is this still the case as my GP is saying I can't be tested again as I have already tested negative?

If your mitochondrial doctor suspects, based on your collection of symptoms and other investigations such as biochemistry, that you could have a mitochondrial condition. However genetic testing done some years ago did not find a gene alteration that confirms your diagnosis (this is still the case for some patients). It could be worth approaching your specialist doctor again to review your case and find out if there are any new genetic tests available for mitochondrial disease that could now be done.

Our knowledge and understanding of the genes that cause mitochondrial disease, including the discovery of new genes, and the technology used to test these genes are evolving all the time.

Why is it important to have an eye check if already blind, and a heart check if known to have LHON?

Eye checks not only assess vision (and it is helpful to have regular eye checks to help you maintain any remaining vision or help prevent it from declining further) but can also detect other health conditions that may affect your eyes. You eye specialist can also give you advice about how to make the best use of whatever vision you have and provide additional support and guidance to relevant services.

I have read a Lily funded research paper which looked at different combinations of nucleosides and their impact on cells from POLG patients; the results were very interesting. What are the next steps / plans?

Unfortunately we were not able to answer this question at the Patient Information event and the Lily team present were also not sure. We suggest you check out The Lily Foundation website for research updates. From a more general point of view, moving trials from the laboratory to the bedside (preclinical to clinical trials) is a lengthy process and requires appropriate funding to be in place.

Can red light therapy help the optic nerve in LHON?

Red light therapy appears to improve mitochondrial function and the survival of cells in experimental models. One previous study did not seem to benefit affected LHON patients, but further work is required.

If I was born with mito, why is it getting worse with time?

There are lots of reasons why your mitochondrial disease may get worse over time. Generally, these are progressive disorders meaning once symptoms have become apparent, they do seem to continue or worsen. The natural aging process involves progressive mitochondrial dysfunction which will also contribute to your disease features. We also known that any metabolic stress on the body, for example an intercurrent illness, can worsen or progress a mitochondrial disease as the cells are not able to cope with the extra demand put upon them.

Why is all the info on LHON focused on eyesight rather than other life impacts?

LHON, Lebers Hereditary Optic Neuropathy, was first defined as a condition in 1871 by an ophthalmologist in Germany (Theodor Leber) with patients who developed sudden painless loss of central vision. The vast majority of patients with LHON genetic variants only develop eye symptoms which is why there is lots of information about the eye features. However, in rare cases the genetic variants causing LHON can affect the nervous system and/or the heart. This is sometimes referred to as Lebers+. There are several published articles about the non-visual manifestations of LHON (Lebers+) and over time we acquire more information about the natural history of the condition.

My child has been diagnosed with chronic idiopathic thrombocytopenia (ITP - low platelets) and we wondered whether this is likely to be connected to his mitochondrial diagnosis of HUPRA syndrome?

There is one published case report of a child with HUPRA having low platelets, but the information and evidence is currently limited. It is important to exclude other, treatable, causes of ITP and not to assume it is associated with the mitochondrial disease. Signing up for the MitoCohort Study allows us to monitor large groups of patients in the UK with mitochondrial disease and to look at the natural history of mitochondrial conditions. Sometimes we can spot patterns or similarities that have not been previously described, which allows us to look at certain features in more detail.

What would trigger medical professionals to start investigating for mito?

Although every case needs to be managed individually, investigations are usually commenced when there is a collection of symptoms that are not explained by another cause, or when there is a known family history of a mitochondrial condition. Certain combinations of clinical features prompt medical professionals to instigate investigations as these combinations would be unusual in other conditions. In children, developmental regression (the loss of previously acquired skills) raises the suspicion of

mitochondrial disease especially if occurring alongside of clinical features unexplained by another condition.

Are there any particularly promising treatments on the horizon?
There are several promising treatments currently being investigated which may benefit patients with mitochondrial disease. Please check out the list of studies funded by The Lily Foundation as well as research studies registered on bepartofresearch.nihr.ac.uk and clinicaltrials.gov

Is there much research re: red therapy?
Red light therapy may help improve mitochondrial function and there are several preclinical and clinical studies in progress. Professor Poulton presented some local research on Red Light Therapy at our Patient Information Event (September 2024) on the effect of red light therapy on muscles. There is also a Lily Foundation funded research study run by Professor Glen Jeffrey and the team at UCL looking at the potential for red light treating ptosis in children.

Would it be possible to have a Zoom webinar or video copy of the research update given at the last Lily Family Weekend as we were not able to attend?
Yes! The Lily Foundation are working on this and will upload to their website soon.

Is there a UK website which lists all UK research projects relating to mitochondrial disorders and with links to each project, where technical information can be viewed?
In addition to the research page on The Lily Foundation website, you can also look up research studies on the following websites:

Be Part of Research

ClinicalTrials.gov

Is it beneficial to continue to exercise as much as possible to try and combat depletion of general muscle strength?

- Yes, it is beneficial to exercise a little and often to maintain muscle strength and encourage mitochondrial activity. Each person is individual in their ability to exercise (lifestyle/work/wellbeing).
- Graded exercise programmes are best as they avoid “Boom and Bust” issues. Exercises usually start at low intensity and are gradually increased.
- Pacing: breaking activities into smaller units and then building into larger units.
- It is advised that you check with your Mitochondrial Physiotherapist if you have any specific heart /exercise tolerance/specific weakness issues that may limit different types of exercise (such as high intensity training).

On the other hand, if it causes excessive fatigue on occasions can it be detrimental to continue exercise…

- During exercise you should feel comfortably out of breath but still able to talk and should not feel pain more than 48hrs post exercise
- If you have an infection/temperature/severe fatigue check with your Physiotherapist first
- Fatigue management is a balance of nutrition/hydration to provide energy and efficient use through graded activities. Remember different activities use up different amounts of energy.