Muscular Dystrophy UK

Fighting muscle-wasting conditions

Mitochondrial myopathy

Overview

Mitochondrial myopathy – or mitochondrial disease – is an umbrella term for conditions caused by faulty mitochondria.

There are several different types, including:

- Kearns-Sayre syndrome (KSS)
- chronic progressive external ophthalmoplegia (CPEO)
- Leber hereditary optic neuropathy (LHON)
- mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS)
- myoclonus epilepsy associated with ragged-red fibres (MERRF)
- Leigh disease
- Mitochondrial DNA depletion syndrome, including Alpers syndrome.

Mitochondria are small structures found inside our cells that are responsible for energy production. Just like a power generator, they take in fuel (the food we eat) and use oxygen to convert it into energy. If this process fails, the cell is unable to work properly and this can lead to mitochondrial disease.

Mitochondrial disease can affect many different parts of the body, particularly those that require a lot of energy such as muscle, brain, nerve, heart, liver and pancreas. Some people with mitochondrial disease have muscle weakness, and they may be given the diagnosis of mitochondrial myopathy

Symptoms

Symptoms can occur at any age, and their severity can vary between individuals (even within the same family).

Mitochondrial disease affects people in different ways. The most common problems are mild weakness of the arms and legs, droopy eyelids (ptosis) and difficulty in moving the eyes (ophthalmoplegia). Others may have exercise intolerance, which means weakness of the arms and legs gets worse after physical exertion. This may also include nausea, headache, light-headedness and heart palpitations.

In severe cases, muscle weakness may be obvious, especially in small babies who may be very 'floppy' (hypotonia) and have difficulty breathing and feeding. Some forms of mitochondrial disease affect the brain. This can lead to developmental delay and/or loss of skills (regression) in children (such as in Leigh disease), epilepsy, stroke-like episodes and progressive loss of memory. Not all mitochondrial myopathies with brain involvement get worse, but some will. The light-sensitive membrane at the back of the eye (the retina) may also be affected and hearing difficulties are common.

Heart problems are common, so doctors recommend regular check-ups. Some patients may develop a very slow heart rate and this may require a pacemaker – an electrical device that helps the heart to beat properly. Certain forms of mitochondrial disease put individuals at risk of developing diabetes, kidney problems, liver dysfunction or other organ problems. Therefore, ongoing management and follow-up need to be tailored to individual patients.

It is important to have a regular intake of calories during the day. If this becomes difficult – in the case of young children, or if you're fasting voluntarily or because of illness – there will be increased demand on mitochondria. Certain drugs may also affect mitochondrial function and specialists generally recommend limiting alcohol. If you're in any doubt, consult your doctor.

Causes

Mitochondrial disease is genetic, meaning it is caused by mutations in our DNA. While most of our DNA is contained within chromosomes in the control centre (nucleus) of our cells, a very small amount (approximately 0.5 percent) is found within our mitochondria. We inherit mitochondrial DNA only from our mothers, whereas nuclear DNA comes from both parents.

Mutations in either nuclear or mitochondrial DNA can cause mitochondrial disease. The inheritance of mitochondrial disease is complex and depends on the location of the mutation.

If the mutation is in the mitochondrial DNA, a mother may pass this on to her children. Men do not pass on a mutation within their mitochondrial DNA. In other words, while both males and females can be affected by mitochondrial disease, only females can pass the mitochondrial DNA mutation on to their children.

If the mutation is in the nuclear DNA, it can be inherited from either parent. (For more information on patterns of inheritance, see our Inheritance factsheet). Some genetic mutations can occur by chance, without any family history. It is important that your specialist tells you about your specific mutation and explains its inheritance.

Diagnosis

When the doctor examines you, certain things may suggest a mitochondrial myopathy, for example droopy eyelids (ptosis), difficulty moving the eyes (ophthalmoplegia), muscle weakness and difficulty with exercise, early onset deafness, balance problems (ataxia), young onset stroke associated with epilepsy, diabetes mellitus and thickened heart muscle (hypertrophic cardiomyopathy).

Looking at a family tree and the clinical symptoms can help determine which type of mitochondrial disease you may have. For some patients, if their clinical symptoms match a readily recognised

condition, such as MELAS or MERRF, the genetic mutation causing mitochondrial disease can sometimes be identified in a blood or urine sample.

Sometimes a muscle biopsy is required for diagnosis. This involves a doctor or nurse removing a small piece of your muscle for further laboratory tests. (You can read more about this in our Muscle biopsies factsheet.)

Under the microscope, mitochondria from people with mitochondrial myopathies often look different from those of a healthy person. They may accumulate around the edges of muscle cells, altering the shape of the muscle cells and giving the so-called 'ragged' appearance. It is also possible for clinicians and scientists to measure how well a patient's mitochondria are working and identify where the defect is. In many cases, it is possible to establish the diagnosis by looking for the genetic mutation in either the mitochondrial DNA or nuclear DNA.

Is the condition life-threatening and will it affect my life span?

There are great variations in mitochondrial myopathy, so it is important to ask your doctor about this.

In many adults affected by mitochondrial disease, the condition progresses slowly. It can sometimes lead to difficulty with everyday activities in later life. Life span may be no different from that of the general population. Specialist input can substantially improve the impact of severe brain involvement, heart problems, major gut problems and breathing difficulties, which would otherwise shorten life span.

Some forms of mitochondrial disease, such as Leigh disease, begin very early in life and can often be life-limiting.

Survival has substantially improved in recent years, which is likely to be a result of better information and targeted supportive care. Most specialist centres issue patients with personalised log books, emergency information sheets or contact details for their specialists. It is strongly recommended that you carry these with you at all times.

Can I avoid passing a faulty gene on to my child?

This is a complex question and the advice will vary depending on both the individual and the type of mitochondrial disease. It is essential to seek advice from a geneticist, a doctor working in one of the specialist centres, or a genetic counsellor that explains your particular diagnosis and whether and how it runs in families. They can explain the range of options available to you, can take you through the pros and cons, refer you to the appropriate centre and give you a route whereby they can answer any further questions.

In cases where the disease is inherited from the mother, the use of eggs (oocytes) from an unaffected donor removes the risk of passing on mitochondrial disease. The donor should not be a maternal relative (such as a sister).

Prenatal diagnosis for mutations causing mitochondrial disease is currently available in the UK. This can reliably diagnose unborn children with mitochondrial diseases inherited from both

parents, and can be used for some but not all maternally-inherited mitochondrial DNA diseases.

Pre-implantation genetic diagnosis (PGD) is also available in the UK. This is widely used for preventing many different genetic conditions being passed on, and as a result, thousands of healthy babies have been born. It is an IVF treatment that allows selection of embryos at no or low risk of developing mitochondrial disease. This can reliably diagnose embryos with mitochondrial diseases inherited from both parents, and works well for many, but not all maternally-inherited mitochondrial DNA diseases. You can read more about prenatal diagnosis and PGD in our Genetic counselling and family planning factsheets.

Mitochondrial donation is a groundbreaking IVF treatment (developed with research funds from MDUK) that reduces the risk of a mother passing on a mitochondrial DNA mutation to her future children. Research studies suggest that mitochondrial donation is both safe and effective in preventing mitochondrial disease, although the long-term effect has not yet been observed. The first baby resulting from using this technique was born in 2016. At seven months the baby was observed to be healthy, and remains under long-term management by healthcare professionals.

This technique is now available in the UK, but it is still early days and as of 2017 no babies have been born in the UK with this method. The technique is currently only suitable for women who are likely to pass severe mitochondrial DNA disease onto their children. Speak to your geneticist, neurologist or GP to discuss your options.

What if I am already pregnant when I am diagnosed?

If you are pregnant, it is important to let your specialist team know this as soon as possible. You may be offered prenatal diagnosis after 11 weeks of pregnancy, if this is available for your condition. Your specialist team can support you through the pregnancy by ensuring your local obstetric team are aware of any potential risks of complications for you or for the baby on delivery.

What should I do during my pregnancy?

It is important to attend antenatal care, maintain a well-balanced diet and avoid extreme weight gain. Depending on the type of mitochondrial disease you have, specialist advice from a dietician may be beneficial. Avoid fasting and excessive exertion. The level of physical activity you take will depend on how severely your muscles are affected. For those able to exercise, it will improve wellbeing and in some cases, lead to improved heart and muscle function.

Your local care advisor can give you practical support and information. They also help families liaise between the various professionals, such as physiotherapists, occupational therapists, social workers and teachers.

Treatment

Although there is no cure for mitochondrial myopathy, many of the problems associated with it can be treated effectively.

For instance, you can treat diabetes with tablets or insulin, epilepsy with anti-epilepsy medications, deafness with hearing aids (or in some cases, cochlear implants), heart rhythm

problems with pacemakers.

You can improve muscle fatigue with regular gentle exercise. The condition can improve in a few patients with specific vitamins such as ubiquinone (coenzyme Q10) and riboflavin, but not in most.

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Here for you

The friendly staff in the care and support team at the Muscular Dystrophy UK's London office are available on 0800 652 6352 or info@musculardystrophyuk.org.

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