

## Mitochondrial Myopathies

### What are mitochondrial myopathies?

Mitochondrial myopathy is a collective term for a group of diseases that particularly affect muscle, but which may also affect every other part of the body including the brain and the eye. Other names for these diseases include: Kearns-Sayre Syndrome (KSS), Chronic Progressive External Ophthalmoplegia (CPEO), Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like Episodes (MELAS), Myoclonus Epilepsy Associated With Ragged-Red Fibres (MERRF), Leigh's disease, and Mitochondrial Cytopathy.

### Why do I have it?

Our bodies are made up of many different tissues, for example muscle, nerve, and liver. Each tissue is composed of small 'building blocks', called cells, and within each cell are small objects known as *mitochondria*. The job of these mitochondria is to produce energy. Just like a power generator, they take in fuel (the food we eat) and burn it up to generate energy. If this process fails, the cell cannot function adequately and this can lead to disease. Muscle and brain require a lot of energy, and are often the most severely affected.

The part of mitochondria concerned with energy production is called the *respiratory chain*. Components (called proteins) of this respiratory chain pathway are produced from a genetic blueprint (the DNA) found either within the mitochondria themselves (mtDNA), or on the chromosomes in what is called the nucleus of the cell. Many mitochondrial diseases, even though they involve the mitochondrial DNA, are sporadic. This means that only one individual in a family is affected – the parents and any children of that person are unaffected. Other mitochondrial diseases are only inherited from the mother. Diseases that arise because of defects within the genes found on chromosomes within the nucleus may be inherited from either parent.

### How did they diagnose me?

When the doctor examines you, certain things may raise the possibility of a Mitochondrial Myopathy, for example droopy eyelids (ptosis), or difficulty moving the eyes (ophthalmoplegia), there is a separate Muscular Dystrophy Campaign (MDC) fact sheet covering Ocular Myopathies. A blood test may show a raised lactic acid level. The final diagnosis often depends on taking a muscle biopsy – where the doctor removes a small piece of muscle for further laboratory tests. Under the microscope, mitochondria from people with mitochondrial myopathies often look abnormal, and they accumulate around the edges of muscle fibres giving the so-called 'ragged red' appearance. It is also possible to make measurements of how well the respiratory chain functions and identify where the defect lies. In some cases it is possible to establish the diagnosis by looking for the defect (we call the mutation) in the genetic blueprint (either mtDNA or nuclear DNA).

### **What happens to people with mitochondrial myopathies?**

Mitochondrial myopathies affect people in different ways. The most common problem is a combination of mild weakness of the arms and legs together with droopy eyelids (ptosis) and difficulty in moving the eyes (ophthalmoplegia). Others only have weakness of the arms and legs, which gets worse after exertion. This may be associated with nausea and headache. If the illness is severe, muscle weakness may be obvious in small babies, and they may have difficulties with swallowing and feeding. Less commonly, some of these conditions affect the brain. This can lead to epilepsy (fits) and progressive loss of memory. Not all individuals with brain involvement (called encephalopathy) get worse, but some will. The light-sensitive membrane at the back of the eye (the retina) is often affected (abnormal pigment accumulates) and hearing difficulties are common. In addition the heart may be affected requiring the insertion of a pacemaker - an electrical device that helps the heart to beat properly.

### **Is the condition life threatening and is my life span going to be affected?**

The most common mitochondrial myopathy, Chronic Progressive External Ophthalmoplegia (CPEO), is usually only a mildly disabling disorder with normal lifespan, whilst others, that begin early in life, are life threatening. Some, such as Leber's Hereditary Optic Neuropathy (LHON), affect only vision. The presence of epilepsy, heart involvement and breathing difficulties are all associated with greater risk.

### **Is there a treatment or cure?**

There are no miracle cures. Many of the problems associated with mitochondrial myopathies can, nevertheless, be treated effectively. For instance, diabetes can be treated with tablets or insulin; pacemakers are very effective for the disturbances of heart rhythm. Muscle fatigue can be improved by regular gentle exercise. A few patients improve on treatment with specific vitamins such as ubiquinone, but most do not.

### **Are there any special risks involved?**

Energy demand increases when we are ill. Fasting, either voluntarily or because of illness, also increases the demand put on mitochondria. Regular intake of calories during the day is, therefore, important. If this becomes difficult, particularly during illness and/or if the patient is a young child, you should contact your doctor. Certain drugs may affect mitochondrial function, and we generally recommend avoiding alcohol. If in doubt you should consult your doctor.

### **Are any other members of my family at risk?**

Recent research has provided a lot of information about the genetic aspects of mitochondrial myopathies and the risk to other family members depends on the precise diagnosis. Most people with mitochondrial myopathies do not have similarly affected relatives, but these are reported in about 20%. Mitochondrial myopathies can be inherited (passed from parent to child) and the genetic error (mutation) can affect either the mitochondrial DNA or the genes found in the nucleus. In those individuals with defects in mtDNA, inheritance will be through the mother whilst for those defects affecting genes in the nucleus either parent may be able to transmit the condition.

**What if I want another baby? 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 disease (for example whether it is transmitted from the mother or the father). In cases where the disease comes from the mother, the use of eggs (oocytes) from an unaffected donor eliminates the risk of transmission, though of course the donor should not be a maternal relative such as a sister. It is possible in certain types of mitochondrial myopathy, to analyse the baby's placenta (CVS), or even the very early embryo (pre-implantation diagnosis), but this is neither widely available nor applicable to all of these disorders.

Your local genetics clinic should be able to advise further. In the case of Leigh's disease, where a mutation has been identified in the affected child, prenatal diagnosis will usually be possible with planned help from specialist centres.

**What if I am already pregnant?**

There is no easy way during pregnancy to assess how severely the baby will be affected for most mitochondrial diseases (see above).

**What can I do to help myself (my child)?**

A good diet, including adequate vitamin intake and the avoidance of obesity are important. Since fasting increases demand on mitochondria, regular meals with, if possible, a high proportion of carbohydrate is recommended. Excessive exertion should be avoided. What level of physical activity you take will depend on how severely your muscle is affected, but for those able to exercise, this will improve well being and in some cases lead to improved muscle function. Our Regional Care Advisers can provide practical support and information. They also help families liaise between the various professionals e.g. physiotherapists, occupational therapists, social workers and teachers.

**Mito Links**

A support group run by people with the conditions and their families, providing support, information and links with other families affected by these conditions.

Web: [www.communicate.co.uk/ne/mitolinks](http://www.communicate.co.uk/ne/mitolinks)

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