

## Minicore (multicore) myopathy

Minicore myopathy, also called, multicore myopathy and multiminicore myopathy, falls under the umbrella of congenital myopathies. These are a group of conditions characterised by muscle weakness and wasting.

Minicore myopathy is a rare condition, and is so named because of the presence of core structures in the muscle fibres. There are four subgroups of minicore myopathy, each with varying symptoms and severity. There is currently no cure for minicore myopathy, but management of the condition is very important and includes physiotherapy, ventilation and corrective surgery where appropriate.

Minicore myopathy is sometimes called multicore myopathy, or multiminicore myopathy, and may also be abbreviated to MmD.

### What causes minicore myopathy?

Minicore myopathy is often inherited in an autosomal recessive pattern. This means that both parents must carry the genetic error for their child to be affected, although neither parent is affected. Both males and females can be affected. Around half of cases of minicore myopathy are caused by a genetic error in one of two genes- Selenoprotein N1 (SEPN1) and Ryanodine receptor 1 (RYR1).

**SEPN1.** Errors in this gene account for around 30% of all cases of minicore myopathy. The gene is located on chromosome 1 and produces a protein called Selenoprotein N1. This gene is also associated with rigid spine muscular dystrophy, and it is now believed that the severe form of classic minicore myopathy and rigid spine muscular dystrophy are the same condition.

**RYR1.** Some of the non-classic forms of minicore myopathy are associated with errors in the RYR1 gene. This gene is located on chromosome 19 and produces a protein which functions as a calcium channel in muscle. Errors in this gene are also associated with central core disease and a condition called malignant hyperthermia (MH). Core structures are also often seen in the muscle of people with central core disease. An overlap of the pathological appearance of what are two genetically distinct conditions may complicate the diagnosis.

People with an error in the RYR1 gene, may also be susceptible to the condition malignant hyperthermia. This is an acute reaction to certain anaesthetics or muscle relaxants used for general anaesthesia. Symptoms of MH include high fever, muscle rigidity, dark brown colouration of urine and acute renal failure. MH is potentially fatal if not treated immediately with dantrolene, but can be prevented by avoiding the triggering agents. This should be brought to the attention of the consultant if surgery is to be considered.

Often cases are sporadic, with no previous family history, and the exact cause of the condition is not known.

More information on genetic inheritance is available in the factsheet 'Inheritance and the muscular dystrophies'.

### **What are the common features?**

There are four subgroups of minicore myopathy.

**Classic form.** This form accounts for around 75% of cases of minicore myopathy. Onset is usually at birth or within the first few months, and presents with floppiness (hypotonia) and delay in achieving motor milestones. Sometimes young infants can have problems with feeding and a feeding tube may be required. Most children are able to walk independently by 28 months. There is generalised weakness, although weakness of the muscles around the trunk and neck are more severe, and curvature of the spine (scoliosis) is common. There are often problems with the respiratory muscles, causing difficulties with breathing.

**Progressive form with hand involvement.** This form affects less than 10% of cases of minicore myopathy. It is less severe than the classic form and scoliosis and respiratory problems are mild or absent. The characteristic feature is that people with this form are double-jointed (hyperlaxity).

**Antenatal form with arthrogryposis multiplex congenita (AMC).** This form also affects less than 10% of people with minicore myopathy. The general feature is the presence of tightened joints (contractures) at birth, due to poor foetal movement. This form is also associated with a range of physical features including long head, low set ears, and a short neck. The respiratory muscles can be moderately to severely affected, thus problems with breathing are common.

**Ophthalmoplegic form.** The main characteristic of this form is external ophthalmoplegia. This is a condition which results in weakness of the muscles around the eye. This can lead to problems with eye movement and sometimes droopiness of the eyelids (ptosis). Along with the weakness around the eyes, there is weakness of the muscles closest to the trunk of the body.

### **How is it diagnosed?**

**Muscle biopsy.** This is done in one of two ways: either a small piece of muscle is taken under general anaesthetic or a needle biopsy is performed to remove a small sample. The sample will be analysed under a microscope.

Muscle tissue from a person with minicore will have a characteristic pattern. Normal muscle tissue has two different types of fibre; type 1 and type 2. Muscle from people with minicore myopathy has more type 1 fibres than type 2. Also, within these fibres, there are structures which are called 'cores'; which can be seen under the microscope. These structures are not specific to minicore myopathy, and so the clinical signs must be considered together with the muscle sample to give a diagnosis of minicore myopathy. A fact sheet on *Muscle biopsies* is available from the Information and Support Line.

**Molecular testing** is currently not available for minicore myopathy. It may be available for families where the specific genetic error has been identified, but a genetic testing centre would have to advise whether this was possible.

### **What other tests are available?**

Since genetic testing is not available for this condition, prenatal diagnosis is also not available. In families where the error has been identified, both prenatal diagnosis and carrier testing may be possible, but a genetic testing centre would have to advise whether this was the case.

### **How will it progress?**

Progression in minicore myopathy is very variable between individuals. In some people the condition remains static, whilst in others muscle weakness may worsen with time.

Sometimes, individuals with the classic form of minicore myopathy may have progressive scoliosis and may show a decline in respiratory function. In most of these cases the course becomes stable in late childhood and many people continue to walk into adulthood, despite scoliosis and the requirement for respiratory support through ventilation.

### **Is there a treatment?**

Currently there is no treatment for minicore myopathy although management of the condition is very important.

**Physiotherapy.** The primary aim of an individual with a neuromuscular disorder is to increase or at least maintain function and mobility. Physiotherapy can assist in doing this, and it can also maintain breathing capacity, delay the onset of curvature of the spine (scoliosis), and help prevent the development of contractures. It is important that the physiotherapist involved is familiar with the treatment of people with neuromuscular disorders.

**Exercise.** There is debate over whether people with neuromuscular disorders should undertake strenuous physical exercise. Some say that putting additional strain on already weakened muscles will cause additional harm, whilst others believe that the exercise may increase muscle strength. Insufficient evidence exists to support either, but it is believed that moderate non-weight bearing exercise such as swimming, walking or peddling may be the best solution. This sort of aerobic exercise helps to maintain a healthy cardiovascular system and a steady weight. It is however, important that this is discussed fully with a clinician.

**Ventilation.** Breathing problems are common with minicore myopathy, and thus respiratory function should be regularly monitored. A decrease in oxygen intake can lead to, among other things, headaches, breathlessness, poor appetite and disturbed sleep. Night time ventilation involves the use of a face mask attached to a small machine, which assists in breathing. This aids the muscles which control breathing, and allows a greater intake of oxygen.

Night time ventilation may be beneficial to people with minicore myopathy, but this should be discussed fully with a consultant to determine whether it is appropriate. If there is a tendency to chest infections it is worth considering pneumovax and the flu vaccine.

**Corrective surgery.** Scoliosis, or curvature of the spine, is common with minicore myopathy. Spinal surgery aims to correct the posture by realigning the spinal column, and involves the insertion of rods, screws or wires. There are benefits and risks associated with this surgery,

and more information is available from the Information and Support Line. As with other treatments, it is very important that the options are discussed fully with a consultant or specialist, before a decision is made. In young children a spinal brace may be used and in children who do not walk moulded seating is used.

**Feeding tube (or gastrostomy).** This is a tube that goes into the stomach through the stomach wall and enables a person to be given food and fluids by passing them directly into the stomach via the tube. People with a myopathy may have problems with swallowing which can lead to choking and inhalation of food. This can result in chest infections. A feeding tube prevents this from happening. There are a number of different types of feeding tube which are available, and these are fitted by a short surgical procedure. A fact sheet on *Gastrostomy* is available from the Information and Support Line.

### **Is there a cure?**

Currently there is no cure for minicore myopathy although much research is currently being conducted into all the congenital myopathies. Although there is no effective treatment to halt the progression, there are a couple of different ways in which to manage the symptoms of minicore myopathy and these are outlined above.

### **What research is currently being done?**

Researchers world-wide are exploring many avenues in an attempt to develop more effective treatments and hopefully a cure. The research department at the Muscular Dystrophy Campaign, regularly monitors research advances in congenital myopathies, and produces releases which are sent to members when significant scientific advances occur.

Email: [research@muscular-dystrophy.org](mailto:research@muscular-dystrophy.org)

### **Planning for the future?**

Since the progression of minicore myopathy is very variable, planning for the future may be difficult. Depending on the severity of the condition there are things which may have to be considered, such as:

- Education
- Holidays
- Ventilation
- Transport
- Home adaptations

Further information on these subjects can be obtained from the Information and Support Line.

### **Other things to consider**

**Anaesthetics and muscle relaxants.** As mentioned, there is an association between minicore myopathy caused by RYR1 mutations and a condition called malignant hyperthermia, which is

triggered by the administration of anaesthetics and muscle relaxants. It is important that this is brought to the attention of the consultant and the anaesthetist if surgery is being considered.

**Medical alert card.** It is very important that health professionals are aware of your condition should you require treatment. There are often issues they will have to consider. Many companies are able to provide a Medic Alert Card, which can be carried to advice of any medical condition. These come in the form of bracelets, pendants etc and carry essential information.

### Where can I get help?

#### **Muscular Dystrophy Campaign**

61 Southwark Street

London SE1 0HL

Tel: **020 7803 4800** (all departments)

Freephone: **0800 652 6352**

Information and Support Line: [info@muscular-dystrophy.org](mailto:info@muscular-dystrophy.org)

#### **Contact a Family**

209-211 City Road,

London EC1V 1JN

Tel: **020 7608 8700**

Helpline: **0808 808 3555** or Textphone: **0808 808 3556**

Email: [info@cafamily.org.uk](mailto:info@cafamily.org.uk)

Web: [www.cafamily.org.uk](http://www.cafamily.org.uk)

#### **Other factsheets that may be useful**

- Myopathy
- Congenital myopathies
  - Central core disease
  - Congenital fibre type disproportion
  - Myotubular (centronuclear) myopathy
  - Nemaline (rod) myopathies
- Mitochondrial myopathies
- Ocular myopathies
- Anaesthetics
- Inheritance and the muscular dystrophies
- Muscle biopsies
- Surgical correction of spinal deformity in muscular dystrophy and other neuromuscular disorders

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