



# Myotubular (centronuclear) myopathy

## Myotubular (centronuclear) myopathy

Myotubular, or centronuclear, myopathy falls under the umbrella of congenital myopathies. It is characterised by a specific pattern in the muscle tissue when viewed under a microscope. There are three different types of myotubular myopathy, described according to the pattern of inheritance seen. Each of these is very rare. There is currently no effective treatment or cure for myotubular myopathy, but management of the condition is very important and includes physiotherapy, and where necessary the use of ventilation and/or a feeding tube.

## What is myotubular myopathy?

Myotubular, or centronuclear, myopathy belongs to the family of congenital myopathies which are characterised by muscle weakness. Congenital means “from birth” and myotubular myopathy is generally apparent very early in life. Myotubular myopathy is so named because of the presence of structures that look like myotubes, immature muscle cells.

## What causes it?

There are three different types of myotubular myopathy each defined by the pattern of inheritance seen. There are also sporadic cases where there is no previous family history, but the prevalence of these has not yet been determined.

## X-linked myotubular myopathy (or XMTM)

This is the most common form of myotubular myopathy, and is caused by an error in the myotubularin (MTM1) gene which produces a protein called myotubularin. This protein is known to be required in muscle development, for the formation of adult muscle.

The MTM1 gene is located on the X chromosome. Individuals have 46 chromosomes, two of which are called the sex chromosomes. Females have two copies of the X chromosome whilst males have one copy of X and one copy of the Y chromosome. If a female has an error on one copy of her X chromosomes, usually she will have enough protein from the “good” chromosome to compensate for the error, and will not have the condition. Manifesting carriers are the exception to this rule (see later section).

If males have the error on their X chromosome, they have no “good” gene to compensate and they will have the condition.

This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

Version 2 / Date published: August 2006 / Original author: MDUK Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician, Robert Jones & Agnes Hunt Hospital, Oswestry / Updated: April 2008 / Date of review: November 2011 / Registered Charity No. 205395 and Registered Scottish Charity No. SC039445



## Autosomal dominant myotubular myopathy

This pattern of inheritance is very rare and only a few families have been described with this condition. The gene abnormality causing the condition was very recently identified by researchers in Paris; it is called the Dynamin 2 gene (DNM2). Autosomal dominant inheritance means that only one copy of the genetic error is needed to cause the condition, and one good copy cannot compensate. This form of the condition affects both males and females.

## Autosomal recessive myotubular myopathy

This pattern of inheritance is also very rare. As with the autosomal dominant form, the gene involved has not been identified, but is expected to have a similar function to the myotubularin gene.

Autosomal recessive means that, in order for a person to be affected, he or she must have two copies of the genetic error. Each parent must carry a copy of the error, but usually they do not show any signs of the condition. This form of the condition also affects males and females.

More information on genetic inheritance is available from the Information and Support Line (contact details shown below).

## What are the common features?

### X-linked myotubular myopathy (or XMTM)

This is the most severe form of myotubular myopathy. It generally affects only males, and has the earliest onset. Commonly there are signs of the condition before the baby is born, and often an excessive accumulation of amniotic fluid around the baby is seen. Most individuals are born with severe floppiness (hypotonia), muscle weakness, and infants may fail to breathe spontaneously at birth, most will require breathing support. There are usually problems with feeding, in particular swallowing, and breathing problems can persist. Chest infections may occur frequently. The child may have a long face, which could seem expressionless. The eyelids may be puffy, and some of the muscles in the eyes may not function correctly. There may be tightening of the knee and ankle joints (contractures).

The severity of the condition varies considerably. In many cases death occurs in the first few months. Some children who survive infancy may show improvement in the first few years, although many will be severely disabled. Many of these children will require ventilatory support to assist their breathing. Occasionally, some children improve significantly and are left with only mild residual weakness even into adulthood.

This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

Version 2 / Date published: August 2006 / Original author: MDUK Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician, Robert Jones & Agnes Hunt Hospital, Oswestry / Updated: April 2008 / Date of review: November 2011 / Registered Charity No. 205395 and Registered Scottish Charity No. SC039445



## Female manifesting carriers of XMTM

Manifesting carriers of myotubular myopathy are very rare. As mentioned earlier, every female has two copies of the X chromosome. In every cell, one copy is “switched off”. Usually this is random, but in some exceptional cases, more copies of the “good” chromosome are inactivated. In such cases a female may show signs of the condition, but this is likely to be only mild weakness.

## Autosomal recessive myotubular myopathy

This is the intermediate form, with onset occurring in infancy or early childhood. Weakness of the muscles in the face may occur, as may droopiness of the eyelids. Some people may have problems with feeding. There is usually weakness of the proximal muscles (those closest to the trunk of the body).

## Autosomal dominant myotubular myopathy

Onset of this form is very variable, ranging from birth to 30 years. It is not as severe as X-linked, and the condition generally follows a mild course. There is weakness of the muscles closest to the trunk of the body, although some people may show weakness of the more distal muscles. A problem with the heart has been seen in one person previously, and so is rare. It is, however, important to regularly monitor heart and lung function.

## How is it diagnosed?

The clinical signs are usually the first indication that there is a problem with the muscles. In order to confirm the diagnosis a muscle biopsy is required.

**Muscle biopsy** - This is done in one of two ways: either an open biopsy where small piece of muscle is taken under general anaesthetic or a needle biopsy is performed under local anaesthetic to remove a small sample. The sample will be analysed under a microscope. Muscle from people affected by myotubular myopathy shows a characteristic pattern, similar to that seen in foetal muscle. The nuclei are centrally located (hence the name centronuclear) instead of being at the outer edges of the fibres. A factsheet on muscle biopsies is available from the Information and Support Line (contact details are shown below).

**Molecular testing** - This is only available for X-linked myotubular myopathy, testing for the dynamin mutation will become available in the future. It seems likely that the genetic cause for the X linked form will be identified in the future. DNA testing involves taking a blood sample and analysing the DNA for the presence of a mutation. The gene is either “read” from end to end, and this sequence is compared to a normal MTM1 sequence, or only certain sections of the gene are analysed. This process can take up to several weeks to complete. Once this error has been identified in one family member, it is possible to use this sequence to diagnose other family members.

This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

Version 2 / Date published: August 2006 / Original author: MDUK Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician, Robert Jones & Agnes Hunt Hospital, Oswestry / Updated: April 2008 / Date of review: November 2011 / Registered Charity No. 205395 and Registered Scottish Charity No. SC039445



## What other tests are available?

Prenatal diagnosis is available for families that are known to have a history of X-linked myotubular myopathy. The technique is described in the section Molecular testing, but there are two ways to obtain samples for testing:

Amniocentesis is traditionally performed at 15 to 17 weeks into the pregnancy. Using ultrasound to visualise, a needle is inserted through the abdominal wall, and a sample of the fluid surrounding the baby (amniotic fluid) is taken.

Chorionic villus sampling (CVS) is carried out at 10 to 11 weeks. This involves taking a sample of tissue from the placenta. Results are available earlier using this technique than amniocentesis, but the rate of spontaneous abortion is slightly higher.

**Carrier testing** - As with prenatal diagnosis, carrier testing is currently only available for families known to be affected by the X-linked form of myotubular myopathy.

## How will it progress?

Myotubular myopathy is a non-progressive or slowly progressive condition. However, infants with X-linked myotubular myopathy may progress into respiratory failure rapidly and the majority of those who survive beyond infancy are dependent on artificial respiration. The autosomal forms are usually less severe.

## Is there a treatment?

There is currently no effective treatment for myotubular myopathy, but management of the condition is very important for prolonging life.

**Night time ventilation** - Breathing problems can occur with myotubular 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 myotubular myopathy, but this should be discussed fully with a consultant to determine whether it is appropriate.

**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 factsheet on gastrostomy is available from the Information and Support Line.

This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

Version 2 / Date published: August 2006 / Original author: MDUK Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician, Robert Jones & Agnes Hunt Hospital, Oswestry / Updated: April 2008 / Date of review: November 2011 / Registered Charity No. 205395 and Registered Scottish Charity No. SC039445



**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.

**Antibiotics** - Chest infections are common with myotubular myopathy and complications with breathing can lead to a variety of other problems, including lethargy, headaches, and poor appetite. Antibiotics are used to treat chest infections. There are a variety of antibiotics available, and a GP will be able to advise on the most suitable. If there is a tendency to chest infections it is worth considering pneumovax (prevenar in children under two years) and the flu vaccine.

## Is there a cure?

Currently there is no cure for myotubular myopathy although much research is being conducted into the congenital myopathies, including myotubular. Although there is no effective treatment for the condition, there are a couple of different ways in which to manage the symptoms of myotubular 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 Muscular Dystrophy UK, regularly monitors research advances in the congenital myopathies, and produces research updates, which are sent to members when significant scientific advances occur.

For more information about research contact Muscular Dystrophy UK Information and Support Line by email or by telephone:

Tel: 020 7803 4800

Freephone: 0800 652 6352

Email: [info@musculardystrophyuk.org](mailto:info@musculardystrophyuk.org)

This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

Version 2 / Date published: August 2006 / Original author: MDUK Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician, Robert Jones & Agnes Hunt Hospital, Oswestry / Updated: April 2008 / Date of review: November 2011 / Registered Charity No. 205395 and Registered Scottish Charity No. SC039445



## Planning for the future?

Myotubular myopathy, although thought to be non-progressive, may change with time, especially as the child grows. This means that the needs of individuals with the condition may change over time.

## There are a number of things which should be considered:

- ▶ Wheelchairs
- ▶ Home adaptations
- ▶ Education
- ▶ Ventilation
- ▶ Holidays

More information on any of these topics can be obtained by contacting the Information and Support Line.

## Other things to consider

**Anaesthetics** - It has now been recognised that the use of general anaesthetics in people with neuromuscular disorders, can cause a variety of different problems. Although anaesthetics are generally well tolerated by people with myotubular myopathy, due to the nature of the anaesthetic drugs used, problems can include dysfunction of the heart, and relaxation of the muscles round the lungs causing problems with breathing. Generally if a patient is properly assessed and monitored, the risks associated with anaesthetic use are low, but it is very important that the medical professionals involved are fully aware of the muscle condition.

**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 advise of any medical condition. These come in the form of bracelets, pendants etc and carry essential information. Please contact the Information and Support Line for details of the companies that provide alert cards.

## Other factsheets that may be useful

- ▶ Carrier detection tests and prenatal diagnosis of inherited neuromuscular conditions
- ▶ Gastrostomy
- ▶ Inheritance and the muscular dystrophies
- ▶ Muscle biopsies
- ▶ Surgical correction of spinal deformity in muscular dystrophy and other neuromuscular disorders

This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

Version 2 / Date published: August 2006 / Original author: MDUK Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician, Robert Jones & Agnes Hunt Hospital, Oswestry / Updated: April 2008 / Date of review: November 2011 / Registered Charity No. 205395 and Registered Scottish Charity No. SC039445



We're here for you at the point of diagnosis and at every stage thereafter, and can:

- ▶ give you accurate and up-to-date information about your or your child's muscle-wasting condition, and let you know of progress in research
- ▶ give you tips and advice about day-to-day life, written by people who know exactly what it's like to live with a muscle-wasting condition
- ▶ put you in touch with other families living with the same muscle-wasting condition, who can tell you about their experiences
- ▶ tell you about – and help you get – the services, equipment and support you're entitled to.

If you would like your GP or other health professional to have more information about Myotubular myopathy, we have some relevant materials. We've developed an online training module for GPs, as well as one for physiotherapists working with adults with muscle-wasting conditions. Contact our helpline or email us to find out more.

If you have feedback about this factsheet please email [info@muscular dystrophyuk.org](mailto:info@muscular dystrophyuk.org).

#### Disclaimer

*While every reasonable effort is made to ensure that the information in this document is complete, correct and up-to-date, this cannot be guaranteed and Muscular Dystrophy UK shall not be liable whatsoever for any damages incurred as a result of its use. Muscular Dystrophy UK does not necessarily endorse the services provided by the organisations listed in our factsheets.*

## 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@muscular dystrophyuk.org** from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

If they can't help you, they are more than happy to signpost you to specialist services close to you, or to other people who can help.

**[www.muscular dystrophyuk.org](http://www.muscular dystrophyuk.org)**

This factsheet is under review, due for updating later in 2017. If you have any queries, please contact us.

Version 2 / Date published: August 2006 / Original author: MDUK Research Department, in association with Dr Ros Quinlivan, Consultant Paediatrician, Robert Jones & Agnes Hunt Hospital, Oswestry / Updated: April 2008 / Date of review: November 2011 / Registered Charity No. 205395 and Registered Scottish Charity No. SC039445