



Ullrich congenital muscular dystrophy

What are congenital muscular dystrophies (CMDs)?

The CMDs are a group of conditions that share an early presentation and a similar appearance of the muscle. Congenital means 'from birth', and in CMDs, the initial symptoms are present at birth or in the first few months of life. They are a very varied group of conditions. Much effort has gone into defining the subtypes and identifying the genes responsible for these specific forms of CMD.

What is Ullrich congenital muscular dystrophy (UCMD)?

UCMD is a form of congenital muscular dystrophy with specific features:

- ▶ the joints of the hands and feet have 'bendiness' or 'hyperlaxity', while the elbows, hips and knee joints have 'contractures' or 'tightness'
- ▶ the spine can have a curvature (scoliosis) or rigidity (stiffness)
- ▶ respiratory muscle weakness and insufficiency develops over time, with the need for night-time non-invasive ventilation by the mid-teenage years.

There are three genes responsible for UCMD: they are called COL6A1, COL6A2 and COL6A3, and they carry the genetic blueprint that is used to produce a protein called collagen VI.

What are the first signs?

Children with UCMD often have hypotonia (low muscle tone or floppiness) and reduced movement at birth. There may be a history of decreased foetal movement during pregnancy, as well. Other common signs are hip dislocation(s), a tendency to hold the head to one side (torticollis), contractures (tightness) in the hips, knees and elbows and notable 'bendiness' or 'hyperlaxity' of the hands and feet.

Sometimes the first signs are only noted after a few months, when babies are observed to have poor head control or have a delay in achieving motor milestones, such as sitting unaided, crawling or walking.

Is UCMD inherited?

Yes. The pattern of inheritance is either 'autosomal recessive' or 'autosomal dominant'. 'Autosomal recessive' means that both copies of one of the collagen VI genes are mutated. This is often caused when both parents are carriers of the condition, meaning the parents have a single mutated gene and, while they do not experience symptoms, they can pass the mutated gene on to their children. If both parents are carriers of the condition, they have a risk of 25 percent – or one in four – of passing the condition on to their children in each pregnancy.



Conditions caused by 'autosomal dominant' mutations require only one copy of a gene to be mutated. These mutations are often 'de novo', which means the genetic change occurred spontaneously in the child and is not carried by either parent.

Sometimes, cases that appear to be caused by 'de novo mutations' are associated with a small risk (approximately one percent) that a parent may carry the condition (via a genetic mechanism known as 'germline mosaicism'), but this is rare. Given the complexity of genetic diagnosis and inheritance patterns, all families of children with UCMD should be referred for genetic counselling. Your neurologist or GP will be able to give you a referral for genetic counselling.

How is UCMD diagnosed?

The diagnosis of UCMD is usually suspected from the clinical history of the person, and an examination of their symptoms. The specific diagnosis, however, is generally made by looking at a piece of muscle or skin (muscle or skin biopsy – see our factsheet: *Muscle biopsies*).

Before doing a muscle biopsy, which involves taking out a small piece of muscle, usually from the thigh, a few other tests may be done. One of these tests is a blood test to measure the level of a muscle protein, called creatine kinase (CK). In patients with UCMD, the CK level is either normal, or mildly elevated.

A **muscle ultrasound** test may also help to detect abnormalities in the muscle. This technique is very simple – similar to the ultrasound tests carried out in pregnancy – and may provide further evidence of the involvement of the muscle.

Muscle magnetic resonance imaging (MRI), as with muscle ultrasound, can assist by highlighting patterns of muscle involvement, which can be specific to particular muscle conditions.

A **muscle biopsy** enables a sample of muscle to be studied under the microscope, looking for signs which might indicate a muscular dystrophy; these include a variation in muscle fibre size and the replacement of some fibres by fat and fibrous tissue. It is also possible, under the microscope, to look at the production of collagen VI in the muscle. There are specific 'markers' or 'tags' that detect whether or not collagen VI is present at normal or reduced levels. A reduction in collagen VI in a child with some of the symptoms of the condition strongly suggests the possibility of UCMD.

As collagen VI is normally present in both muscle and skin, a **skin biopsy** (taking a small piece of skin) can also help to confirm the diagnosis of UCMD. In some cases, it is easier to detect a reduction of collagen VI in skin cells than it is in muscle cells. A skin biopsy, however, does not provide some of the information that can be obtained from a muscle biopsy and, therefore, it is important to have both muscle and skin biopsies, when UCMD is suspected.



Genetic tests, looking for mutations in one of the three genes responsible for UCMD (COL6A1, COL6A2 and COL6A3), are now available in the UK at a specific designated centre, and can provide a definitive diagnosis. If you would like to have these genetic tests, ask your neurologist consultant for a referral to the nearest place to you.

Prenatal diagnosis may be possible in UCMD. In families who already have a child with UCMD and decide to have another baby, it is possible to detect whether or not the foetus (unborn child) has a deficiency of collagen VI and/or the same gene mutation(s), early in the pregnancy.

Is there a treatment or cure?

At present, there is no cure for UCMD but there are ways, described below, of helping to alleviate the effects of the condition. Research into the CMDs is however developing and holds the promise of future, early-stage clinical trials testing potential treatments for some of the symptoms of the condition

Can a child with UCMD learn to walk?

The severity of this condition varies greatly from person to person. Some children learn to walk but may lose this ability over time. Some children with UCMD may have the ability to walk on their knees only, while other children may not have the ability to walk independently at all.

What other physical effects might UCMD have on a child?

As the muscles are weak and mobility is limited, the child may be born with – or develop – joint ‘contractures’. This means that the muscle tendons tighten up and the child is unable to move the limbs or the joints as freely as a healthy child would. Physiotherapy can help prevent or slow the progression of these contractures, so it is helpful for parents to work with a physiotherapist, soon after diagnosis, to establish a programme of exercises for their child to do daily at home.

Hips are commonly affected by contractures and may sometimes be dislocated. Children with UCMD should be assessed by an orthopaedic specialist with expertise in muscle-wasting conditions, ideally working as part of a multi-disciplinary team alongside a paediatric neurologist and a physiotherapist. Some children may require treatment with a splint or, in some rare cases, surgery.

Most children with UCMD also develop a curvature of the spine (scoliosis). This should be monitored in a specialist spinal clinic and may require a spinal brace to improve posture and slow deterioration of the curvature. Surgical intervention (scoliosis surgery) might be needed in some cases.

As collagen VI is also normally present in the skin, children with UCMD have a tendency for scars to heal slowly or become thickened and elevated (keloid formation).



Is UCMD progressive and is it life-limiting?

In the first few years, the condition is fairly stable and the child usually appears to gain strength and achieve motor milestones, albeit delayed. Over time, and particularly with increased growth during puberty, children typically demonstrate more difficulty walking. Children may also experience loss of independent walking as early as seven years of age or as late as the late teenage/early adult years (in those children with the 'intermediate' form of the condition).

Children experience breathing problems while sleeping because the muscles that assist breathing are affected. It is essential, therefore, to monitor lung function on a regular basis by performing respiratory function tests; overnight 'sleep studies' are also regularly required. Night-time breathing problems can also cause children to feel tired during the day, have headaches on waking in the morning, have a loss of appetite and lose weight.

A decrease in lung function can also result in frequent chest infections. If these signs are present, or if the level of oxygen recorded during an overnight sleep study is not satisfactory, children need to be referred to a respiratory specialist to initiate night-time non-invasive ventilation (NIV). This entails a special facial or nasal mask attached to a small machine that pumps air into the lungs and maintains adequate ventilation. It may also be needed when children develop chest infections.

Another problem frequently encountered by children with UCMD after the first few years of life, is difficulty feeding. This can result in prolonged mealtimes and failure to gain weight normally. For this reason, it is essential to monitor weight and height to ensure children with UCMD receive enough food and energy.

Some children with UCMD may need to take nutritional supplements. A small surgical procedure called a gastrostomy can be performed, which entails inserting a tube directly into the stomach. Gastrostomy tube-feeding ensures people with UCMD receive an adequate level of nutrition when they cannot consume sufficient calories orally.

What help is available?

Physiotherapy is one of the main forms of help. An initial physiotherapy assessment at the time of diagnosis should be followed by an exercise programme and regular check-ups. The main aim of physiotherapy is to keep the muscles as active as possible and to prevent or slow the progression of joint contractures. People with UCMD are encouraged to remain as active as possible. Swimming is a particularly good form of exercise.

Physiotherapists can also help provide orthoses, such as splints, long leg callipers and a wheelchair when necessary.

Children and adults with UCMD should ideally be followed regularly in a specialist neuromuscular clinic, with access to a multi-disciplinary team including physiotherapy, orthotic, respiratory, orthopaedic, spinal and genetic specialists as needed.



Other related publications

This factsheet is to be used alongside the following publications:

- ▶ Congenital muscular dystrophies
- ▶ MDC1A (merosin-deficient congenital muscular dystrophy)
- ▶ SEPN1-related myopathy
- ▶ Bethlem myopathy
- ▶ Carrier detection tests and pre-natal diagnosis
- ▶ Inheritance and the muscular dystrophies
- ▶ Muscle biopsies
- ▶ Surgical correction of spinal deformity in muscular dystrophy and other neuromuscular disorders

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 Ullrich congenital muscular dystrophy, 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.

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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@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