Merosin-deficient congenital muscular dystrophy

What is merosin-deficient congenital muscular dystrophy?

The congenital muscular dystrophies (CMDs) are a group of conditions that share an early presentation and a similar appearance of the muscle. Congenital means 'from birth,' and in congenital muscular dystrophy, the initial symptoms are present at birth or in the first few months. The CMDs are a very varied group of conditions, and much effort has gone into defining different subtypes of congenital muscular dystrophy and to identifying genes responsible for these specific forms of CMD. Merosin-deficient congenital muscular dystrophy (MDC1A) is one of the subtypes of CMD.

How is MDC1A caused?

The gene responsible for causing MDC1A was the first gene identified that causes congenital muscular dystrophy. The gene, called LAMA2, carries the genetic information required to produce the laminin-□2 protein, which is a key component of the muscle protein called merosin.

How is MDC1A diagnosed?

MDC1A is usually suspected based on the person's clinical history and an examination of the symptoms. The specific diagnosis is typically made from studies performed on a muscle biopsy. However, a few additional tests may need to be done.

One of these tests is a blood test, which measures the level of a muscle enzyme called creatine kinase (CK). This enzyme is usually found in the muscles, but, following muscle damage, can leak into the bloodstream; in those with MDC1A, levels of CK in the blood are typically elevated (often to more than 10 times the normal values).

All children with MDC1A have a particular constitution of the white matter of the brain which shows, by six months of age, as altered 'white matter signal' on brain imaging. Brain MRI (in which clinicians take photos of the brain in a non-invasive way) may be very helpful in identifying the condition in a child, when muscle biopsy appearances are not typical or when a muscle biopsy is not available.

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A skin biopsy may also be taken to make a diagnosis of MDC1A, since merosin is absent in both muscle and skin in MDC1A. A skin biopsy involves taking a very small skin sample under a local anaesthetic. However, in most instances a muscle biopsy is preferred since it allows the study of many more proteins and enables the diagnosis of MDC1A even in those in whom merosin expression appears normal.

Genetic tests looking for abnormalities in LAMA2, the gene responsible for MDC1A are now available in UK. These are done in a laboratory in a specific nationally designated centre and can provide a definitive diagnosis. If you would like to have these genetic tests, speak to your neurologist consultant about the nearest place to you and ask them to arrange a referral.

Is there a treatment or cure?

At present, there is no cure for MDC1A, but there are ways, described below, of helping to alleviate the effects of the condition. Research into congenital muscular dystrophies is however developing, and it is likely that experimental clinical trials may start in the not-too-distant future.

MDC1A can be helped by timely recognition, professional advice and intervention. It is advisable for people with MDC1A to be regularly followed by a neurologist with expertise in muscle-wasting conditions, ideally working as part of a multi-disciplinary team. Reviews should include monitoring of weight, respiratory function, muscle strength and joint range, with the co-ordination of sleep studies to assess breathing quality during sleep. Annual 'flu immunisations' as well as other vaccinations are advisable to reduce the risk of chest infections.

Children and adults with MDC1A should ideally be followed regularly in a specialist neuromuscular clinic, with access to physiotherapy, orthotic, respiratory, orthopaedic, spinal and genetic specialists as needed.

What is the prognosis?

Children born with MDC1A often have hypotonia (decreased muscle tone or floppiness) at birth, and may have reduced movements and contractures (tightness of the joints) of the hips, knees and elbows. Sometimes the first signs of MDC1A are only noted after a few months when children have difficulties in holding their head up or are delayed in meeting motor milestones, such as sitting unaided, crawling or walking.

In children with a partial reduction of merosin, the degree of muscle weakness may be milder, and some may learn to walk independently, albeit delayed. Children who have the ability to walk may lose this ability as they grow older and heavier, as the muscles may be unable to cope with a greater strain. It is also possible that some individuals with partial merosin deficiency may retain the ability to walk, into adulthood.

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As the muscles are weak and mobility limited, the child may develop or be born with 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. Hips are commonly affected with contractures and may sometimes be dislocated. Most children with MDC1A also develop a curvature of the spine (scoliosis) and require specialist advice about promoting appropriate sitting support, bracing and, if required, surgery.

As mentioned above, all children with MDC1A have changes in the white matter of the brain, which are visible on brain MRI imaging by six months of age. This is not usually associated with problems in cognition (the thinking processes in the brain). However, a minority of children with MDC1A experience seizures, which can usually be well controlled with anti-epileptic medication.

Weakness of the respiratory muscles is a common problem in people with MDC1A and can result in frequent chest infections and hypoventilation at night (shallow or slow breathing). These are potentially serious complications that require both prompt recognition and intervention. Nocturnal breathing problems may happen in children of any age and can result in symptoms of daytime sleepiness, morning headaches after awakening, a poor appetite and weight loss.

Another problem frequently encountered by children with MDC1A 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 MDC1A receive enough food and energy. Swallowing problems can occur, as well, since the muscles responsible for swallowing may be weak. For some people with MDC1A, it may be necessary 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 children and adults with MDC1A receive an adequate level of nutrition when they cannot consume sufficient calories orally.

This factsheet is to be used alongside the following publications:

- Congenital muscular dystrophies
- SEPN1-related myopathy
- Ullrich congenital muscular dystrophy
- Carrier detection tests and prenatal diagnosis of inherited neuromuscular conditions
- Inheritance and the muscular dystrophies
- Muscle biopsies factsheet
- Surgical correction of spinal deformity in muscular dystrophy and other neuromuscular disorders
- An introductory guide for families with a child newly diagnosed with a neuromuscular condition

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Muscular Dystrophy UK
Fighting muscle-wasting conditions

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 merosin-deficient 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.

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 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.musculardystrophyuk.org

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