



## MDC1A (merosin-deficient congenital muscular dystrophy)

### What is merosin-deficient congenital muscular dystrophy?

The congenital muscular dystrophies are a group of conditions which share 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. Congenital muscular dystrophies are a very heterogeneous group of conditions and in the last few years a lot of effort has gone into identifying the separate entities and in locating the gene responsible for a number of these forms.

The gene responsible for merosin-deficient congenital muscular dystrophy was the first gene to be identified in a proportion of patients with congenital muscular dystrophy and lies on chromosome 6 (1p35-p36). This gene is responsible for the production of laminin  $\alpha 2$  which contributes to the protein called merosin.

### Which are the first signs?

Babies with merosin-deficient congenital muscular dystrophy often have hypotonia (decreased muscle tone, floppiness), and may have reduced movements and contractures (tightness) in the hips, knees and elbows. Sometimes the first signs are only noted after a few months when the children have difficulties in holding their head or have a delay in learning new skills such as sitting unaided, crawling or walking.

### Is merosin-deficient congenital muscular dystrophy inherited?

Yes. The pattern of inheritance is known as 'autosomal recessive'. This means that both parents are carriers of the condition (although clinically unaffected) and they have risk of 25%, or 1 in 4, in each pregnancy of passing the condition on to their children.

### How is merosin-deficient congenital muscular dystrophy diagnosed?

The diagnosis of merosin-deficient congenital muscular dystrophy is usually suspected from the history and examination. The specific diagnosis however is generally made by looking at a piece of muscle (muscle biopsy). 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** which measures the level of a muscle enzyme (creatinine kinase or CK) that is generally very much raised (more than 10 times the normal values).

**Muscle biopsy** can provide a precise diagnosis in two ways:

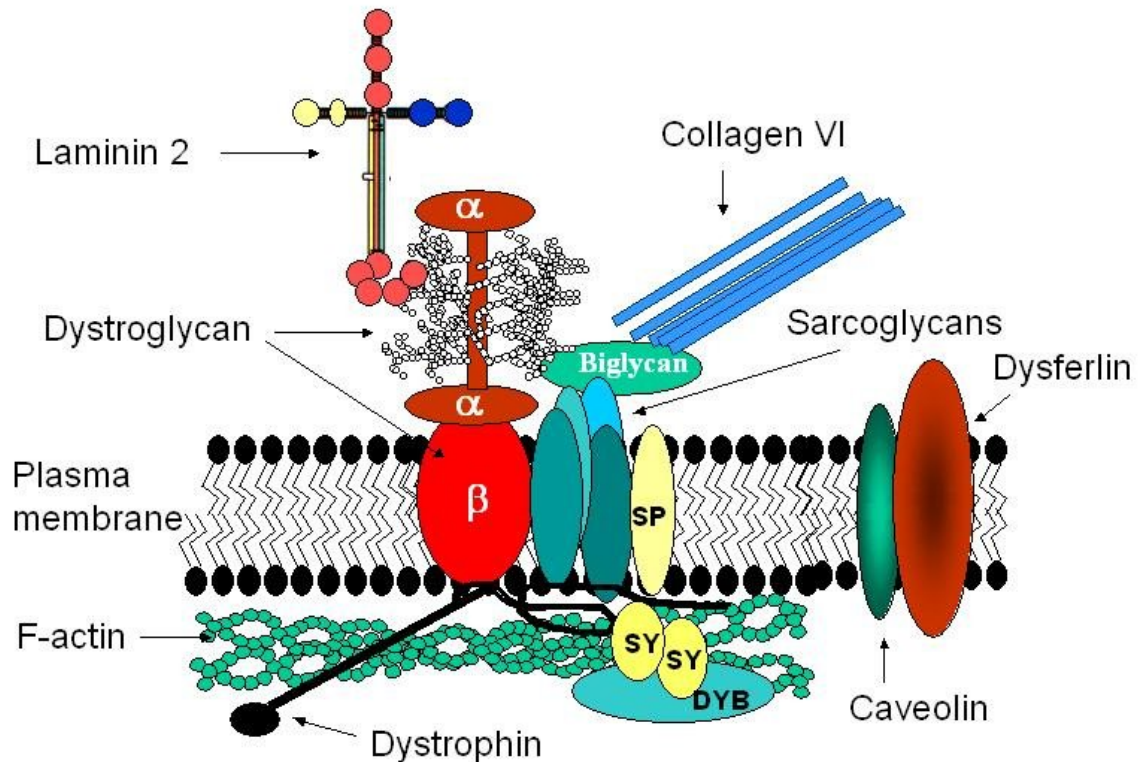
- When the muscle is studied under the microscope, it is possible to look for signs which might indicate a muscle problem. In children with a muscular dystrophy the muscle fibres, instead of being evenly sized, show a great variation and some of these fibres are replaced by fat and fibrous tissue.
- It is also possible to look at the presence of merosin in the muscle under the microscope. There are specific 'tags' which can interact with merosin and detect whether this protein is

normally present or reduced. A reduction in merosin in a patient with evocative clinical features strongly suggests the possibility of MDC1A.

In MDC1A a **skin biopsy** rather than a muscle biopsy may also be used. This followed the discovery that the protein merosin, normally present in both skin and muscle, is absent in both tissues in patients with MDC1. A skin biopsy means only having to remove a very small skin sample from the patient and

may be done under a local anaesthetic. However in most instances a muscle biopsy is preferred as it allows the study of many more proteins and therefore diagnose forms in which merosin is normal.

The following illustration shows where merosin is present in muscle:



In the upper part of the illustration, a number of relevant extracellular proteins and their interactions are shown. Laminin 2 interacts, among other proteins, with dystroglycan. Dystroglycan is in turn associated, intracellularly, with the protein dystrophin.

**Genetic tests** looking for abnormalities in the gene responsible for MDC1A congenital muscular dystrophy are now available in a NSCAG laboratory and provide the ultimate diagnosis.

**Prenatal diagnosis** is a development in the diagnosis of inherited conditions. It is based on the ability to detect the abnormality in the developing fetus. In families who have a child with MDC1 congenital muscular dystrophy who decide to have another baby it is possible to detect whether the baby has the same protein or gene defect early in pregnancy.

**Is there a treatment or cure?**

At the moment there is no cure for congenital muscular dystrophy, but there are ways, described below, of helping to alleviate the effects of the condition.

**Can a child with MDC1A learn to walk?**

The severity of this condition varies. Children in whom merosin is completely absent or is only present in very small traces generally never achieve walking without support. Some of them may be able to stand or to walk using assistance such as long leg callipers.

Some children might have a partial reduction of merosin and a proportion of the effects are milder and they may learn to walk although this may be delayed. Children who have successfully walked may lose the ability later on because as they grow older and heavier, the muscles are unable to cope with a greater strain. On the other hand it is also possible for some of these patients to retain the ability to walk for the entire life.

#### **What other physical effects might MDC1A have on a child?**

As the muscles are weak and mobility is limited, the child may develop or be born with '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. Physiotherapy can help prevent this and a programme of exercises should be worked out with a physiotherapist very soon after diagnosis.

Even a very young baby can be helped to maintain suppleness. Hips are commonly affected and if they are dislocated this may require treatment with a splint or sometimes surgery.

Most of the children with MDC1A also develop a curvature of the spine (scoliosis), this can be helped by promoting appropriate sitting support and, if required, a brace.

All children with merosin deficient congenital muscular dystrophy also have a particular constitution of the white matter of the brain that can be seen following a brain scan. This is not associated with any particular problem in these children and is therefore not a worrying feature, but its presence is often searched for to confirm the diagnosis. Only a minority of children with merosin deficient congenital muscular dystrophy have seizures. These are usually well controlled with drugs, if present.

#### **Is MDC1A progressive and is it life threatening?**

Motor function remains relatively stable but when children reach puberty, and grow taller and heavier, children might experience additional difficulties.

A very common problem in patients with MDC1A is weakness of the respiratory muscles, giving rise to frequent chest infections and hypoventilation (poor breathing) at night. Both are

potentially serious complications that need to be promptly recognised and acted upon. It is therefore very important to monitor respiratory function during the night by checking oxygen levels on a regular basis, usually once a year. This test is very simple and consists of applying a small wrapping around one finger. The wrapping is connected to a small machine recording the level of oxygen throughout the night. Night time breathing problems may happen in children of any age and when present, children feel tired, often have headaches in the morning, soon after they wake up, may feel sleepy during the day and lose some weight. If these signs are present or if the level of oxygen recorded at night are not satisfactory, children can be helped by referring them to a respiratory physician who will provide a mean of supporting breathing at night (ventilator). This usually requires a special facial or nasal mask attached to a small machine that pumps air when it is needed.

Another frequent problem after the first few years is failure to thrive and it is therefore also important to monitor weight and height to be sure that these children receive enough food and energy. Very often there are also problems in swallowing as the muscles which are responsible for swallowing are weak. In several cases feeding supplements are needed. Sometimes a small surgical procedure called gastrostomy can be performed to help the child to receive the appropriate level of feeding via a tube directly into the stomach and maintain his/her weight.

#### **Where can I get help?**

##### **Muscular Dystrophy Campaign**

61 Southwark Street

London SE1 0HL

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

Freephone: **0800 652 6352**

Email addresses:

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

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

**Contact a Family**

209-211 City Road,

London EC1V 1JN

Tel: **020 7608 8700**

Fax: **020 7608 8701**

Helpline: **0808 808 3555** or

Textphone: **0808 808 3556**

Freephone for parents and families (10am-4pm, Mon-Fri)

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

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

**Other MDC factsheets that may be useful**

- Congenital muscular dystrophies
  - Rigid spine syndrome
  - Ullrich congenital muscular dystrophy
- Carrier detection tests and prenatal diagnosis of inherited neuromuscular conditions
- Inheritance and the muscular dystrophies
- Muscle biopsies

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