

Congenital Muscular Dystrophy

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What is Congenital Muscular Dystrophy?

The term Congenital Muscular Dystrophy (CMD) was first used in 1908 to describe a condition in which infants exhibit muscle weakness from birth. *Congenital* means present at birth, while *muscular dystrophy* refers to muscle weakness and degeneration.

CMD is used to describe a group of disorders that are initially characterized by abnormally decreased muscle tension, deformed joints, and generalized weakness. It is a rare disorder, affecting males and females equally, at a rate between 7-12 per 100,000 births

Extensive and ongoing research in the area of muscular dystrophies is promising, however there is currently no known cure for CMD. Intervention is directed towards helping CMD patients to enjoy the quality of life that others may take for granted.

What are the features of Congenital Muscular Dystrophy?

Signs of CMD include general muscle weakness and joint deformities. More severe forms of CMD may include severe mental and speech problems, and seizures.

Several researchers have proposed classifications for CMD. The following scheme from Muntoni and Voit (2004) is comprehensive, defining four categories of CMD:

Defect:	Type of CMD:
Extracellular matrix protein defects:	<ul style="list-style-type: none"> • Laminin-alpha2-deficient CMD (MDC1A) • Ullrich CMD (UCMD 1, 2, 3)
Integrin-alpha7 deficiency (ITGA7)	
Glycosyltransferases (abnormal O-glycosylation of alpha-dystroglycan)	<ul style="list-style-type: none"> • Walker-Warburg syndrome • MEB disease • Fukuyama CMD (FCMD) • CMD + secondary laminin deficiency 1 (MDC1B) • CMD + secondary laminin deficiency 2 (fukutin related protein deficiency, MDC1C) • CMD with mental retardation and pachygyria (mutation in LARGE, MDC1D)
Proteins of the endoplasmic reticulum – rigid-spine syndrome (RSMD1)	

Laminin-alpha2-deficient CMD (MDC1A) is the most common CMD, and accounts for approximately 40% of all cases. Reduced fetal movements in utero may be noticed. At birth, patients may have low

muscle tone (hypotonia), weakness, difficulties in feeding, and respiratory problems. Contractures are common. External ophthalmoplegia (paralysis of the motor nerves of the eye) may occur late. Most infants eventually sit unsupported, but standing is rare. Nerve disorders (demyelinating neuropathy) are common, and CNS manifestations may be present, such as mild mental retardation, seizures and structural brain changes. Weakness is usually static, or minimally progressive. Complications are related to respiratory compromise, feeding difficulties, scoliosis, and cardiopulmonary disease.

Typical features of **Ullrich CMD** include presentation in the neonatal period with hypotonia, kyphosis (curvature) of the spine, contractures, torticollis (twisting of the neck), and hip dislocation. Protruding heel bones (calcaneus) may be exhibited, as well as hyperlaxity of the joints. Kyphosis and the contractures may improve with therapy, and some patients will learn to walk in time, or with delay. However, this ability to move around independently will be lost after 2-10 years, usually due to recurring contractures. Respiratory insufficiency invariably develops within the first ten to twenty years. Children with CMD are often characterised by facial dysmorphism, including micrognathia, a round face with prominent ears and drooping of the lower lid. Brain function is normal, as is cardiac function.

Integrin-alpha7 deficiency is extremely rare; only three children in the world have been diagnosed with this condition.

FCMD is usually picked up in utero, by poor fetal movements. A weak mouth and lack of head control is noticeable in the neonatal period. Between two and eight years of age, most children with FCMD can stand or walk a few steps, but some patients may require support to even sit. In most cases, cardiac disease develops after 10 years of age, resulting in cardiomyopathy and congestive heart failure. Eye abnormalities are present in about 50% of patients, and cerebral changes are always present, resulting in seizures for many patients. Severe mental retardation is present, although many children with FCMD do learn to talk. Death from muscular weakness and respiratory failure usually occurs mid-teens, although this varies from two to 25 years of age.

MEB disease is variable in its severity. Severely affected children cannot sit or turn, and they lack visual contact. These children do not usually live past the first one to two years. Moderately affected patients can often sit, and speak a few words. They may have severe short-sightedness (myopia), but can make visual contact. Mildly affected children may be able to walk for a short time, they can speak in sentences, and they have good vision. Seizures are common in MEB disease, as is mild-to-severe mental retardation. Mild-to-severe brain changes are common and show up on an MRI. Hydrocephalus (excessive fluid in the brain) may need to be treated with the placement of a shunt.

Walker-Warburg syndrome presents in utero or at birth with hypotonia, weakness in the feeding muscles (difficulties in sucking, swallowing), and contractures. This is a progressive disease, and the average time of death is nine months of age. Eye abnormalities such as retinal detachment and cataracts will lead to blindness. Brain abnormalities are severe and common.

MDC1C is variable in severity and symptoms. The severe end of the spectrum includes muscular dystrophy, eye abnormalities leading to blindness, and structural brain abnormalities. The typical form is similar to CMD with laminin-alpha2 deficiency (MDC1A). Presentation is at birth with hypotonia and weakness with delayed motor milestones. Some children with this disorder will be able to sit up, or take a few steps in the first decade of life, but progressive weakness leads to respiratory insufficiency and death, or ventilatory dependence. Hypertrophy of the tongue and legs will be noted, and facial weakness is usually present. Mild weakness of the heart can occur (cardiomyopathy). Intelligence and brain MRIs are normal. The mild form presents with characteristics similar to that of limb-girdle disease. With early-onset weakness, the ability to walk is lost in the teens, and subsequent scoliosis and ankle contractures occur. Muscle and tongue hypertrophy is common, and facial weakness is common. Teenagers will usually require ventilatory assistance, and respiratory failure is the most common cause of death. With late-onset (in teens or adulthood), walking and mobility can be preserved until the sixth or seventh decade, but respiratory insufficiency and failure may develop before then. Cardiomyopathy develops in 50% of patients with early- or late-onset weakness.

MDC1D has been described in one case, a 17 year old female who presented with weakness and hypotonia at five months of age.

MDC1B patients present in the first year with hypotonia and weakness. Motor milestones are delayed, but walking is achieved by three years. Facial weakness is prominent, and muscle hypertrophy is common. Respiratory failure leads to death or the need for ventilatory assistance. Intelligence and brain MRIs are normal.

RSMD1 is apparent at birth, or within the first year of life with variable degrees of weakness and hypotonia. Most patients will eventually walk and maintain mobility for many years, and in contrast to Ullrich CMD, contractures are not present at birth, but usually develop between the ages of three and ten. Contractures may occur in the limbs, fingers and face. Children with RSMD1 are often characterised by spinal rigidity and scoliosis. Respiratory insufficiency is common and progressive. Ventilatory assistance at night may be needed as early as the first decade. The cardiac system is usually normal, and intelligence and brain function is not affected.

What causes Congenital Muscular Dystrophy?

CMD is a genetic disease, caused by a fault in any number of different genes. Genes contain the recipe for proteins, and when faulty, may result in the reduction or complete absence of the protein. In the case of CMD, the proteins affected are muscle proteins. The reduction or loss of these muscle proteins create the characteristic symptoms of muscle wasting and weakness.

CMD may be inherited, or it may arise spontaneously. Spontaneous or sporadic mutations occur randomly during a child's conception. When the mutation is inherited, it is usually in an autosomal recessive pattern. This means that the condition will only become apparent in a child if both parents carry the faulty gene, yet do not display symptoms. Other forms may be autosomal dominant, and one severe form is X-linked, affecting boy babies.

For further information on genetics and how disorders are inherited, please refer to the *Muscular Dystrophy Association Genetics Factsheet*.

Diagnosis of Congenital Muscular Dystrophy

There are often difficulties in diagnosing CMD, as signs and symptoms of the disease vary. Where there is no family history, CMD is unlikely to be suspected straight away. The earliest sign of CMD is likely to be a 'floppy baby' – severe proximal weakness at birth or within twelve months of birth. Once CMD is suspected, diagnostic tests will be offered to establish a definite diagnosis. These may include:

- **CK Testing**

As in many of the muscular dystrophies, blood levels of the muscle enzyme creatine phosphokinase (CK, or CPK), may be increased. This enzyme is normally found in muscle cells. When the muscle cell is damaged, CK leaks out into the blood stream. A blood test will show elevated levels of CK, up to ten times that of normal.

- **MRI**

Magnetic resonance imaging (MRI) is a technique that is able to generate an image of the soft tissue in the brain. This allows visualization of the characteristic brain changes that occur with some CMD disorders.

- **EMG**

An electromyography (EMG) investigates the electrical activity of a muscle. In CMD, the EMG will typically show activity that is smaller and shorter than usual. Nerve conduction velocity (NCV) tests measure the speed with which a nerve is able to transmit information. This test is more accurate in the older child than in infancy.

- **Muscle Biopsy**

A muscle biopsy is required for diagnosis. Normal muscle fibres are regular in size; in CMD they may appear irregular, or poorly formed. There may be evidence of muscle degeneration and repair.

Soon after the diagnosis of a CMD child, it is essential that genetic counselling is arranged, for one or both of two issues. The first is the probability that the mutation was inherited from the parents; and the second is whether testing for the condition in future pregnancies can be offered, and with what degree of reliability.

- Genetic counselling provides information about possible diagnostic tests, including prenatal testing. Genetic services in NZ are available and a referral can be made by the MDA.

Management of Congenital Muscular Dystrophy

As yet, there is no cure for CMD. It is possible, however, to minimize the complications by adhering to a management programme specially designed by a team of medical professionals. The team will usually be headed by a paediatric specialist, and includes a physiotherapist, together with specialists in other areas as required.

- **Exercise**

Passive exercise, or assisted stretching, should be established as early as possible. It is valuable to have regular contact with a physiotherapist who can assist in the development of an exercise programme to delay the onset of contractures.

- **Supportive Equipment**

Braces and walking sticks may prolong mobility, but it is likely that a motorized or light-weight manual wheelchair will be required. An occupational therapist and/ or seating therapist can advise on the most appropriate type of chair and supportive seating. It may therefore be wise to consider suitability of the home environment at an early stage, so that adjustments can be made over time to make it more wheelchair accessible.

- **Nutrition**

Excessive weight gain can occur due to reduced physical activity produced by the muscle weakness. Being overweight can place extra stress on already weak heart and bowel function, on joints, and also with breathing. It is therefore important that kilojoule intake reflect energy needs. Poor suckling in infancy may mean that feeding tubes are required. There should be no need for extra dietary supplement.

- **Surgery**

If contractures develop at the ankle joints, these can be surgically treated by release of the Achilles tendon. This helps improve foot position. Having a comfortable foot position may help prolong mobility for some CMD children.

Spinal fusion surgery is performed to correct scoliosis. The medical team, including an Orthopaedic Surgeon and headed by the paediatrician, will discuss this option with the CMD boy and his family well before the surgery becomes necessary.

- **Respiration**

As muscles become gradually weaker, respiratory function starts to decline enough to produce changes in the way the lungs pull air in and push it out. Family and caregivers must watch carefully for signs of disrupted sleep due to respiratory problems. Signs include morning drowsiness, lack of concentration, headaches, confusion, sleepiness during the day and wakefulness at night with an increased need to be turned. When respiratory problems become apparent, ventilation machines are available to assist with ventilation during the night.

Research into Congenital Muscular Dystrophy

Current research is specific for the different types of CMD disorders, but is focused on identifying the cause for the genetic mutations.

Considerable resources are being invested in gene therapy at present. Replacing the faulty gene with a normal gene, or a normal gene with a similar function could ultimately prove to be a cure for genetic diseases such as CMD. Such a cure, however, is many years away.

Support for people with CMD

- **Education**

In New Zealand, every child has the right of equal access to all aspects of education. This means that all children with a neuromuscular condition have the right to attend a mainstream school. Many schools have special units attached which can provide any extra help needed, including an individualized education plan for appropriate assistance with physical and mental needs.

- It is important that children with CMD are not overprotected or patronized – they should be mentally stimulated and creative skills encouraged.

- **Employment**

There is no reason why a person with CMD should not expect to have the same employment opportunities as anybody else; however it is probably

prudent to plan a career which will remain suitable even if physical ability declines.

Workbridge provides a professional employment service for all people with all types of disabilities and injuries, no matter what the disability or skill level. Workbridge also administers support funding on behalf of Work and Income. Workbridge can be contacted on free phone: 0508 858 858 or through their website: www.workbridge.co.nz

More help on equal employment rights can be found on the Employment Relations website www.ers.dol.govt.nz. Employment Relations also has an infoline: 0800 800 863.

The government promotes equal employment opportunities (EEO) in private sector employment through the EEO Trust. They can be contacted on (09) 523 3023, or by visiting their website www.eeotrust.org.nz

Remember, it is illegal for employers to discriminate against people because of ethnicity, sexual orientation, gender, marital status, religious belief or disability. Equal rights are demanded by the Human Rights Act, 1993, and the Equal Pay Act, 1972.

More information

Muscular Dystrophy Association can be contacted for further information, assistance, advice, support and referrals, on 0800 800 337 or by e-mail at info@mda.org.nz

The Muscular Dystrophy Association Website also contains information on services available within NZ, our quarterly magazine, contacts, membership details, news and links to other sites - www.mda.org.nz

Further references

www.mdaua.org – the Muscular Dystrophy Association USA website has an extensive site with plenty of further information on any muscular dystrophy conditions as well as research news.

www.muscular-dystrophy.org – the UK muscular dystrophy site. It contains good general information on the condition.

NZ also has an excellent website dedicated to helping and informing those families with rare disorders – www.nzord.org.nz

Information in this fact sheet was primarily sourced from:

Muscular Dystrophy Canada - <http://www.muscle.ca>